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THE NATIONAL CLEARINGHOUSE FOR MENTAL HEALTH INFORMATION

VOL. 13 NO. 2 October 1975

PSYCHOPHARMACOLOGY ABSTRACTS

NATIONAL INSTITUTE OF MENTAL HEALTH

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The Secretary of Health, Education, and Welfare has determined that the publication of this periodical is necessary in the transaction of the public business required by law of this Department. Use of funds for printing this periodical has been approved by the Director of the Office of Management and Budget through December 31, 1976.

ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

198484 Gortinskaya, T. V.; Sinyukhin, V. N.; Ostroumova, N. G.; Rozynov, B. V.; Nyrkova, V. G.; Savitskaya, N. V.; Mashkovskiy, M. D. Vsesoyuznyy nauchno issledovatel0skiy khimiko farmatsevticheskiy institut im. Ordzhonikidze, Moscow **/On the metabolism of a new antidepressant, azaphen, in rats./** O metabolizme u krys antidepressanta azafena. Farmakologiya i Toksikologiya (Moskva). 36(6):673-677, 1973.

The metabolism of azaphen was studied by analyzing the urine of rats injected with this antidepressant. Urine was collected during a 24-hour period following the injections. Three substances were separated out through ascending partition chromatography with silica gel. One of these was unchanged azaphen, the second was azaphen in the form of a demethylated metabolite, and the third was in the form of conjugated glucuronic acid combinations with a chemical structure resembling that of azaphen. Azaphen with the hydroxylated phenol ring and its demethylated metabolite were proposed to be precursors of the glucuronic acid mixture found in the urine. 16 references. (Journal abstract modified)

198605 Lawrence, David K.; Pertwee, Roger G.; Gill, Edward W.; Piper, Julian M. University Department of Pharmacology, South Parks Road, Oxford, England **Brain levels and relative potency of the 1,2-dimethylheptyl analogue of delta1-tetrahydrocannabinol in mice.** Biochemical Pharmacology (Oxford). 23(21):3017-3027, 1974.

Unlabeled and tritium labeled forms of the 1,2-dimethylheptyl analog of delta1-tetrahydrocannabinol (delta1-DMHP) were prepared as incompletely separated mixtures of threoisomers and erythroisomers. The n-heptyl analog was also prepared, and this compound and samples of delta1-DMHP containing different proportions of threoisomers and erythroisomers were compared with delta1-tetrahydrocannabinol (THC) using the mouse ring "catalepsy" test. The major metabolite in the mouse of delta1-DMHP was isolated from an in vitro mouse liver preparation and identified as 7-hydroxy-delta1-DMHP. The brain levels of this metabolite and delta1-DMHP itself correlated equally well with the behavioral effect and showed that the higher activity of delta1-DMHP is not due to metabolic or distribution effects. It is concluded that the differences in potencies of delta1-THC and delta1-DMHP in producing behavioral changes in the mouse are due to differences in activity at the site of action. 19 references. (Author abstract modified)

198608 Niaguchi, Tetsukichi; Inoue, Takako; Sakai, Tokiyasu. First Chemistry Section, National Research Institute of Police Science, Chiyoda-ku, Tokyo, Japan **Studies on the in vitro metabolism of compounds related to lysergic acid diethylamide (LSD).** Biochemical Pharmacology (Oxford). 23(21):3063-3066, 1974.

The in vitro metabolism of several lysergic acid diethylamide (LSD) derivatives by the rat liver 9000 g supernatant was investigated to find some clues to the mechanisms of LSD's hallucinogenic action through study of the metabolic pathways of those derivatives, D-2-bromolysergic acid diethylamide, 1-methyl-D-lysergic acid (+)-butanolamide-(2) (methysergide), D-lysergic acid (+)-butanolamide-(2) (methergine), D-lysergic acid dimethylamide, D-lysergic acid amide, and several isomers of these derivatives were included. It was found that the enzymatic demethylation of LSD derivatives at position six to form nonderivatives was independent of their physiological actions, and that a side chain at position eight of normal LSD derivatives was enzymatically attacked to form monoalkylamides or hydroxyalkyl amides. However, an exception occurs when the compound possesses a methyl group at position one, for then demethylation occurs at position one instead of six. 9 references.

199208 Schultz, Otto-Erich; Reimerdes, E. H. Pharmazeutisches Institut der Christian-Albrecht-Universitat, 23 Kiel, Gutenbergstr. 78, Germany **/HMO analysis of structure activity relations in sedative and hypnotic drugs and analysis of potential sedatives by means of homologous compounds./** HMO-analyse zu den Struktur-Wirkungsbeziehungen von Sedativa und Hypnotika und die Analyse potentieller Sedativa in Form von Homologverbindungen. Arzneimittel-Forschung (Aulendorf). 23(6):776-778,1973.

The simple Huckel molecular orbital linear combination of atom orbitals (HMO-LCAO) method is used for the calculation of structural parameters for the possible structures of barbituric acid and dioxopiperidine derivatives, resulting from the pi electron distribution in these molecules. The calculations include a series of 2-pyrone compounds, which were synthesized and showed partially sedative activity in pharmacological screening. The evaluated parameters, which appear to be responsible for the activity of the the compounds are summarized. 42 references. (Author abstract modified)

200006 Hollett, Charlotte R. Department of Pharmacology, Meharry Medical College, Nashville, TN 37208 **Identification and structural characterization of an inhibitor of catecholamine-induced free fatty acid mobilization from the calf midbrain.** Life Sciences (Oxford). 15(7):1301-1307, 1974.

A substance which inhibits norepinephrine induced free fatty acid mobilization was isolated from the calf midbrain. A preparation of the inhibitor, considered to be highly purified, was resolved into two distinct components by paper chromatography. Both components (designated Fractions I and II) inhibited free fatty acid mobilization in adipose tissue fragments in the presence of norepinephrine. One component (Fraction II) was identical chromatographically to an inhibitor of free fatty acid mobilization prepared from the dog hypothalamus. Fraction II has a molecular weight of 136, and appears to have the structure of a pyridylacetic acid. 3 references. (Author abstract)

200310 Parker, Martin Dale. University of Kentucky **The influence of anions on the physical properties of butyrophenone-type molecules. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-19626 HC$12.50 MF$4.00 121 p.

The effects of ion pair formation on the solubility, oil/water partitioning, aqueous dissolution rate, and gastrointestinal absorption of haloperidol, droperidol, and pimozide were investigated. The order of decreasing pKa, maximum solubility, and pH of maximum solubility was haloperidol, then droperidol, then pimozide. Increasing concentrations of certain anions significantly influenced oil/water partitioning of haloperidol and pimozide but had no effect on droperidol partitioning. Chloride ion caused dramatic decreases in the in

vitro dissolution rate of haloperidol base and haloperidol phosphate in hydrochloric acid solution at pH 2 and in acetate buffer at pH 4.2. Increasing chloride ion had relatively little effect on the dissolution rate of haloperidol hydrochloride in either system. After injecting rats with haloperidol, it was found that in vivo results paralleled in vitro solubility, partitioning, and dissolution rate studies. (Journal abstract modified)

200738 Breyer, Ursula; Prox, Axel; Bertele, Rudolf; Gaertner, Hans Jorg. Institut fur Toxikologie, Universitat Tubingen, D-7400 Tubingen, Germany **Tissue metabolites of trifluoperazine, fluphenazine, prochlorperazine, and perphenazine in the rat: identification and synthesis.** Journal of Pharmaceutical Sciences. 63(12):1842-1848, 1974.

Tissue metabolites of trifluoperazine, fluphenazine, prochlorperazine, and perphenazine were identified and synthesized in the rat. Rats were treated chronically with increasing doses of trifluoperazine, prochlorperazine, fluphenazine, or perphenazine per os, and their metabolites were extracted from rat livers, kidneys, and lungs. Isolation and separation of the compounds were achieved by thin layer chromatography (TLC). Besides the parent drugs and the derivatives formed by removal of the terminal N-alkyl group, tissues contained metabolites resulting from degradation of the piperazine ring to form an ethylenediamine structure. This biotransformation occurred with and without concomitant removal of the terminal N-alkyl group, so that monosubstituted and symmetrically disubstituted ethylenediamine derivatives were produced from each drug. The structures of the metabolites were elucidated by mass spectrometry and confirmed by chemical synthesis. 11 references. (Author abstract modified)

200739 Nudelman, Abraham; McCaully, R. J.; Bell, S. C. Wyeth Laboratories, Inc., Radnor, PA 19087 **Water-soluble derivatives of 3-oxy-substituted 1,4-benzodiazepines.** Journal of Pharmaceutical Sciences. 63(12):1880-1885, 1974.

Several acid addition salts of amino ester derivatives of 3-oxy-substituted 1,4-benzodiazepines were prepared and tested for water solubility, stability, and pH. The monomethanesulfonic acid salts were found most suitable for parenteral administration. 12 references. (Author abstract)

201003 Singhabhandhu, Anamai. Southern Illinois University **Crystal-structure determinations of the donor-acceptor complexes of phenothiazine and phenoxazine with nickel thiete. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-18878 HC$12.50 MF$4.00 136 p.

The crystal structures of donor-acceptor molecular complexes of bis-cis-(1,2-perfluoromethylethylene-1,2-dithiolato) nickel (nickel thiete) with phenothiazine and with phenoxazine were determined. The structure of phenothiazine-nickel thiete consists of stacks of phenothiazine and nickel thiete molecules in a 2:2 ratio configuration. The nickel thiete molecule is relatively planar, while the phenothiazine molecule is bent along the N-S axis to produce a dihedral angle of 172.2deg. The structure of phenoxazine-nickel thiete is composed of alternating phenoxazine and nickel thiete molecules in a 1:1 ratio. The centrosymmetric nature of the structure imposes the oxygen/nitrogen position of phenoxazine to be disordered with half occupancy of each atomic species present. Molecules are nearly planar. The donor-acceptor intermolecular distance is longer than any distance previously reported for donor-acceptor complexes, while the distance of phenothiazine-nickel thiete is within the range of previous reports. (Journal abstract modified)

202312 Bolt, Arthur G.; Ghosh, Peter B. Raymond Purves Research Laboratories, Royal North Shore Hospital, St. Leonards, N.S.W. 2065, Australia **Benzo-2,1,5-oxadiazoles -- a novel class of heterocyclic monoamine oxidase inhibitors.** Biochemical Pharmacology (Oxford). 23(14):1963-1968, 1974.

The in vitro inhibition of monoamine oxidase (MAO) by a series of oxazoles, oxadiazoles, benzoxadiazoles and related heterocycles was tested. An increase in inhibitory activity was observed from the monocyclic oxadiazole, through the bicyclic benzoxadiazole to tricyclic compounds such as naphthfurazan and furoxanobenzofuroxan. Furoxanobenzofuroxan was the most potent inhibitor of the series. 30 references. (Author abstract)

202381 Holmstedt, Bo R. Karolinska Institutet, Stockholm, Sweden **Analysis of psychoactive phenolic amines.** Psychopharmacology Bulletin. 10(1):62, 1974.

Isolation and pharmacologic evaluation of various botanical samples thought to contain phenolic amines are described. Preliminary results include isolation and identification of alkaloids from 13 South American plants, discovery of psychotomimetic agents in the snuff used by some Indian tribes, and development and use of mass fragmentography to identify the intermediate of mescaline and tetrahydroisoquinoline alkaloids. Findings may contribute to a more precise understanding of the chemical action induced by psychotomimetic drugs and reveal new sources of such drugs.

202382 McLaughlin, Jerry L. Purdue University, Lafayette, IN **Search for new hallucinogenic cacti.** Psychopharmacology Bulletin. 10(1):62-63, 1974.

A number of selected cactus species was examined in order to isolate new alkaloids with therapeutic or hallucinogenic properties. About 34 species of North American cacti comprise the subject matter. Thin layer and gas liquid chromatography are used to extract and identify alkaloid substituents. Preliminary results indicate that eight of the nine species of cacti commonly called "peyote" contain hordenine and N-methyltyramine and that certain extracts of the small Mexican peyote cactus, Pelecyphera aselliformis, contain 3,4-dimethoxy-beta-phenethylamine. Ten alkaloids have been isolated from Coryphantha Macromeria, with normacromerine the major compound. Five alkaloids have been isolated from Coryphantha ramillosa.

203027 Vishveshwara, Saraswathi. City University of New York, New York, NY **The structural chemistry of adrenergic neural transmission systems. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-20844 HC$12.50 MF$4.00 136 p.

The results of INDO molecular orbital calculations on the geometries and electronic structures of R(-) norepinephrine, R(-) epinephrine, R(-) isoproterenol, dopamine, erythroephedrine, threo ephedrine, R(-) phenylethanolamine, and phenylethylamine are presented. The conformations predicted to be preferred in the free space approximation are discussed in terms of intramolecular interactions, and the calculated potential energy surfaces and electronic charge distributions for each molecule are considered in terms of crystallographic, spectroscopic and bioassay data. The effect of substituents on various parts of the phenylethylamine molecule are studied in terms of potential energies and electronic distributions. (Journal abstract modified)

204196 Maier, R. D.; Wehr, K. H. Abteilung fur Gerichtliche Medizin, Rhein.-Westf. Techn. Hochschule, D-5100 Aachen, Lochnerstr. 4-20, Germany /**The detection of Prazepam, a new benzodiazepine tranquilizer.**/ Sum nachweis von Prazepam, einem neuen Tranquillizer aus der Reihe der Benzodiazepine. Archives of Toxicology (Berlin). 32(4):341-345, 1974.

Thin layer chromatographic and gas liquid chromatographic data on the benzophenone obtained after acid hydrolysis of prazepam are given. A differentiation from the benzophenones of five therapeutically used benzodiazepines was possible. The structure of the benzophenone was verified by nuclear magnetic resonance spectroscopy as 2-(cyclopropyl-methylamino)-5-chlorbenzophenone. 5 references. (Author abstract)

205029 Post, Michael L.; Kennard, Olga; Horn, Alan S. University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW, England **Possible pharmacological and theoretical implications of X-ray structure of the tricyclic antidepressant imipramine.** Nature (London). 252(5483):493-495, 1974.

The X-ray structure of the tricyclic antidepressant imipramine was investigated in an attempt to gain some insight into the conformational requirements for a compound to be a potent inhibitor of noradrenaline and 5-HT uptake. Two conformations of the solid state structure were identified. Molecular diagrams showing angle values, and potential energy maps demonstrating the possibility of the existence of other conformations of similar energy to the crystal form are included. It is concluded that there is no positive way to determine which conformation is most likely in a noncrystalline form. 23 references.

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

198479 Komendantova, M. V.; Briskin, A. I.; Bakunyaeva, A. G.; Milogradova, G. P. Moskovskiy meditsinskiy stomatologicheskiy institut i laboratoriya farmakologii, Moscow /**The influence of tyrocalcitonin on conditional reflexes and the electrical activity of the brain in animals.**/ Vliyaniye tirokal0tsitonina na uslovnyye refleksy i elektricheskuyu aktivnost0 mozga zhivotnykh. Farmakologiya i Toksikologiya (Moskva). 36(6):645-651, 1973.

The influence of the hormonal preparation, tyrocalcitonin (TKT) on the central nervous system of rats and rabbits was studied. TKT was introduced into the peritoneum intravenously, under the skin and orally. The conditional-defensive reflexes of rats and rabbits going through a labyrinth were measured. The electrical activity of the optic, auditory, and sensory motor areas of the cortex was measured by electrodes. Used in doses producing hypocalcinemia, TKT was found to elicit moderate excitation of the central nervous system. 22 references.

199209 Oelschlager, H.; Behrendt, W. A.; Hoffmann, H. 6 Frankfurt/Main, Georg-Voigt-Str. 14, Germany /**Basic derivatives of diphenylmethane with a depressive effect on the C.N.S.**/ Basische Diphenylmethanderivate mit zentraldepressiver Wirkung. Arzneimittel-Forschung (Aulendorf). 23(6):802-806, 1973.

The synthesis of seven new basic derivatives of diphenylmethane is reported. These compounds bear some structural resemblance to metabolites of those 1,4-benzodiazepines with a tranquilizing effect. Pharmacological screening tests have shown that these substances cause either excitation or depression of the C.N.S. according to the dose administered. These compounds differ from the 1,4-benzodiazepines in having a weaker effect against convulsions caused by pentetrazolum (i.p.), and in a weaker anticonvulsive effect against electroshock. There is no distinctive effect in the taming tests. The specific effect of the 1,4-benzodiazepines seems to be a function of the diazepine ring. 16 references. (Author abstract modified)

199385 Hache, J.; Duchene-Marullaz, P.; Streichenberger, G. Centre Europeen de Recherche Mauvernay, route de Marsat, 63201 Riom, France /**Pharmacological profile of a new non-tricyclic antidepressant: oxaflozane (1.766 Cerm).**/ Profil pharmacologique d'un nouvel antidepresseur non tricyclique: l'oxaflozane (1.766 Cerm). Therapie (Paris). 29(1):81-93, 1974.

Behavioral 2-(3-trials in rats of oxaflozane, 2-(3-trifluoromethylphenyl)-4-isopropyltetrahydro-1,4-oxazine, a nontricyclic antidepressant, are reported. Oxaflozane presents a pharmacological profile of dissociated antireserpinic activity in mice and a marked anticataleptic action and a weak potentiation of stereotypies provoked by amphetamine, reminiscent of antidepressant drugs. The drug also shows a marked antiaggressive activity. This profile, quite different from the tricyclic antidepressants, presents great potential in application to depressive syndromes. 9 references. (Journal abstract modified)

200405 Presley, Jerry Max. University of Mississippi **The effects of chlorpromazine, atropine, morphine and pentobarbital on induced gastric ulceration in rats. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. Mfilms, No. 74-20608 HC$12.50 MF$4.00 183 p.

The effects of chlorpromazine, atropine, (ATP) morphine, and pentobarbital (PBT) on induced gastric ulceration in rats were examined. Chlorpromazine was found to be more reductive than the other drugs. Morphine was significantly more therapeutic than ATP and PBT on three comparisons. The atropine treatment produced significant comparisons for the glandular section of the stomach. In Experiment II, three doses of chlorpromazine, three doses of morphine, and one treatment which was a combination of chlorpromazine and atropine were tested to evaluate their antiulcer properties. The treatments which significantly decreased the number of ulcers were: 4.2mg/kg, 8.5mg/kg, 12mg/kg chlorpromazine, and 5.0mg/kg morphine. (Journal abstract modified)

200564 Zakusov, V. V.; Krolevets, G. N. Laboratoriya farmakologii nervnoy sistemy, Instituta farmakologii AMN SSSR, Moscow /**The influence of trifluoperazine, carbidine and imizine on evoked potentials in different structures of the limbic-reticular complex.**/ Vliyaniye triftazina, karbidina i imizina na vyzvannyye potentsialy v razlichnykh strukturakh limbiko-retikulyarnogo kompleksa. Byulleten0 eksperimental0noy biologii i meditsiny (Moskva). 77(2):44-47, 1974.

The influence of trifluoperazine, carbidine, and imizine on evoked potentials in the limibic-reticular structures of rabbits was investigated with sciatic nerve stimulation. Trifluoperazine and carbidine exerted a pronounced depressing effect on evoked potentials in the centrum medianum, nucleus of the thalamus, posterior nucleus of the hypothalamus, and the median gray matter. The amplitude of evoked potentials increased in the dorsal hippocampus and the amygdala. The changes were more pronounced with trifluoperazine than with carbidine. Imizine exerted a pronounced depressive effect on evoked potentials in the dorsal hippocampus, centrum medianum, nucleus reuniens and the small cell part of the dorsomedian nucleus of the thalamus. Imizine aroused a double phase effect in the amygdala posterior nucleus of the hypothalamus and median gray matter, i.e. an increase in the

amplitude in the first phase and a decrease in the second. In reticular structures of the midbrain, the evoked responses increased more under influence of imizine than of trifluoperazine or carbidine. 13 references. (Journal abstract modified)

201320 Browne, R. G.; Harris, R. T.; Ho, B. T. Texas Research Institute of Mental Sciences, Houston, TX 77025 **Stimulus properties of mescaline and N-methylated derivatives: difference in peripheral and direct central administration.** Psychopharmacologia (Berlin). 39(1):43-56, 1974.

The possibility that N-methylated derivatives of mescaline might produce interoceptive stimuli similar to mescaline was examined in rats. Following the acquisition of response control by i.p. mescaline, the subjects were tested for stimulus generalization after i.p. or intraventricular injections of various doses of mescaline, N-methylmescaline (NMM), N,N-dimethylmescaline (DMM), or saline. Intraventricularly administered mescaline exhibited a dose dependent generalization to the cue produced by systemically injected mescaline, indicating a central nervous system locus of action. NMM demonstrated only saline responses. DMM generated responses characteristic of mescaline suggest a similarity in behavioral effects between DMM and mescaline. However, following i.v. injection of DMM, only a transient generalization to the mescaline state resulted. It is concluded that NMM and DMM do not play a significant role in the mescaline induced internal stimuli. 23 references. (Author abstract modified)

201914 Romanova, L. A.; Sinyukhin, V. N.; Polezhaeva, A. I.; Gorkin, V. Z.; Mashkovsky, M. D. Institut biologicheskoy i meditsinskoy khimii AMN SSSR, Moscow **/The effect of diazaphenoxazine derivatives on monoaminoxidase activity./** O vliyanii proizvodnykh diazafenoksazina na monoaminoksidaznuyu aktivnost0. Farmakologiya i Toksikologiya (Moskva). 37(4):391-393, 1974.

The effect of diazaphenoxazine derivatives on monoamine oxidase activity was studied in vitro and in rats. In neither case did azaphen or other derivatives exert any noticeable effect on monoamine oxidase activity. 9 references. (Journal abstract modified)

202109 Nichols, David E.; Barfknecht, Charles F.; Long, John P.; Standridge, Robert T.; Howell, Henry G.; Partyka, Richard A.; Dyer, Donald C. College of Pharmacy, University of Iowa, Iowa City, IA 52242 **Potential psychotomimetics. 2. Rigid analogs of 2,5-dimethoxy-4-methylphenylisopropylamine (DOM, STP).** Journal of Medicinal Chemistry. 17(2):161-166, 1974.

The potential psychotomimetics, 2-amino-5,8-dimethoxy-6-methyl-1,2,3,4-tetrahydronaphthalene and 2-amino-4,7-dimethoxy-5-methylindan were prepared as rigid analogs of psychotomimetic phenylisopropylamines. Neither compound appeared to have psychotomimetic activity in rats. The effect of the aminotetralin derivative on 5-HT receptors in rat fundus strips and sheep umbilical arteries was also studied. 37 references. (Author abstract modified)

202192 Hollister, Leo E. Veterans Administration Hospital, Palo Alto, CA 94304 **Structure-activity relationships in man of cannabis constituents, and homologs and metabolites of delta9-tetrahydrocannabinol.** Pharmacology (Basel). 11(1):3-11, 1974.

A variety of cannabis constituents and THC isomers, homologs and metabolites were examined for structure-activity relationships. The fundamental structure of THC is required for pharmacological activity, but potency may be altered greatly among different double bond isomers, by changing length of side chain or by metabolic hydroxylations. No material has been found in nature, either in cannabis itself or in the metabolites of THC, which differs qualitatively from THC. 27 references. (Author abstract)

202862 Honma, T.; Sasajima, K.; Ono, K.; Kitagawa, S.; Inaba, Sh.; Yamamoto, H. Takarazuka Research Labs., Sumitomo Chemical Co., Ltd., Takatsukasa, Takarazuka-shi, Hyogo-ken, Japan **Synthesis and preliminary pharmacology of a novel butyrophenone derivative, ID-4708.** Arzneimittel-Forschung (Aulendorf). 24(9):1248-1256, 1974.

A new butyrophenone, 1-(3-(2-amino-4-fluorobenzoyl)-propyl)-4-hydroxy-4-(3-trifluoromethylphenyl) piperazine (ID-4708) was synthesized from 2-methyl-6-fluoroindole by six steps. It is shown that ID-4708 possesses potent antiapomorphine and antimethamphetamine activity in animals, and is two and four times as potent as trifluperidol. The inhibitory activity of ID-4708 on the conditioned avoidance response by a shuttle box test was nearly equal to that of trifluperidol, and its potency was equal or greater in open field tests. The duration of cataleptic activity of ID-4708 was short; it protected powerfully against epinephrine induced death, and its suppression of spontaneous locomotor activity in mice was similar to that of trifluperidol. These and other characteristics indicate that ID-4708 may be a potent neuroleptic with few unfavorable side-effects in clinical practice. 27 references. (Author abstract modified)

204192 Lipp, J. A. Biomedical Section, Defence Research Establishment, Suffield, Ralston, Alberta, Canada **Effect of diazepam upon soman-induced seizure activity and convulsions.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 32(5):557-560, 1972.

To study the effect of diazepam upon soman induced seizure activity and convulsions, monkeys with chronically implanted cortical and subcortical electrodes were given the anticholinesterase compound by intramuscular injection. When the electroencephalograph (EEG) began to exhibit seizure activity accompanied by convulsions, diazepam was administered intravenously. Diazepam produced an immediate decrease in seizure activity and all convulsions were abolished. Atropine, when used alone, failed to control seizure activity or convulsions. All animals were comatose for varying periods following the administration of diazepam and then began to become more alert. The EEG exhibited low voltage fast activity which is characteristic of diazepam. All surviving animals were alert the following day but exhibited some muscular weakness. The EEG was similar to the control record. The combination of diazepam and atropine raised the lethal dose 50 by a factor of two. 16 references. (Author abstract modified)

204862 Gardner, Donald E.; Illing, Joseph W.; Miller, Frederick J.; Coffin, David L. National Environmental Research Center, EPA, Research Triangle Park, NC 27711 **The effect of ozone on pentobarbital sleeping time in mice.** Research Communications in Chemical Pathology and Pharmacology. 9(4):689-700, 1974.

The effect of repeated daily exposure of female mice to ozone (1.0ppm x 3 hours) on pentobarbital sodium (50mg/kg) sleeping time has been studied. Pentobarbital sleeping time for control mice exposed to clean filtered air was 21 minutes. There was a significant increase in sleeping time as a result of prior treatment with ozone. The difference was manifested

consistently when pentobarbital sodium anesthesia followed the second and third exposures. For example, when compared to controls, those exposed for 2 days increased their sleeping time by 18 minutes. No difference was discernible following a single exposure or from four or more successive daily exposures to this same concentration. After seven daily exposures to 1.0ppm, increasing the ozone to 5 ppm for a single 3 hour exposure resulted in a further increase in sleeping time. This one hour exposure increased the sleeping time difference to 59.5minutes as compared to control mice. 29 references. (Author abstract)

204865 Gudelsky, G. A.; McCall, R. B.; Chiueh, C. C.; Moore, K. E. Dept. of Pharmacology, Michigan State University, East Lansing, MI 48824 **Lack of effect of amantadine on d-amphetamine-induced release of dopamine from cat brain in vivo.** Research Communications in Chemical Pathology and Pharmacology. 9(4):653-660, 1974.

To study the effect of amantadine of d-amphetamine induced release of dopamine, the cerebroventricular system of anesthetized cats was perfused with artificial cerebrospinal fluid (CSF) after the intraventricular administration of 3H-dopamine. The perfusate was subsequently analyzed for 3H-dopamine. The addition of d-amphetamine (.01 millimolar) or amantadine (millimolar) to the perfusing CSF increased the efflux of 3H-dopamine from the cat brain. A lower concentration of amantadine (.1millimolar) did not increase the spontaneous efflux of 3H-dopamine nor did it alter the d-amphetamine induced release of this amine. 22 references. (Author abstract modified)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

198135 Maitre, Michel; Ciesielski, Lucien; Lehmann, Alice; Kempf, Eliane; Mandel, Paul. Centre de Neurochimie du CNRS, Institut de Chimie Bioligique, Faculte de Medecine, Universite Louis Pasteur, 67085 Strasbourg Cedex, France **Protective effect of adenosine and nicotinamide against audiogenic seizure.** Biochemical Pharmacology (Oxford). 23(20):2807-1816, 1974.

Intraperitoneal injection of adenosine into Swiss albino mice, RB strain, sensitive to audiogenic convulsions, rapidly produces, in proportion to the dose: sedation, modification of the EEG, lowering of arterial pressure and protection against audiogenic seizures. Simultaneous injection of adenosine and nicotinamide produces the most striking protection, the effect being independent of all others. During the protective period to convulsions, there is an elevation in the energy rich compounds, ATP and phosphocreatine, which is attributable to a reduction in their rate of degradation. During the same period, a diminution in the cerebral level of noradrenaline takes place. The pharmacological effects of adenosine oppose those of its structural analog, caffeine, with regard to mobility, arterial pressure, basal metabolic rate and body temperature. 28 references. (Author abstract modified)

198196 Shankar, R.; Mishra, O. P. Dept. of Biochemistry, Institute of Medical Sciences, Banaras Hindu Univ., Varanasi 221005, India **Effect of reserpine on cationic contents of rat brain.** Nature (London). 251(5475):532, 1974.

The effects of reserpine on cationic contents of the rat brain was studied. The in vitro experiments show that during anaerobic conditions, reserpine greatly enhances the rate of glycolysis by adult rat and guinea pig cerebral cortex slices. It is possible that reserpine may exert this effect indirectly by amine release. Reserpine may also exert its effect on the anaerobic glycolysis by increasing potassium(K)ion/sodium(Na)ion ratio. Reserpine had a significant effect in increasing K ion contents of the cerebral cortex slices incubated under anoxic conditions. It was shown that reserpine may affect the cationic movements. It was also found that chronic reserpine administrations result in an increase in the K ion contents of brain more than 25% while the Na ion contents are not affected. 11 references. (Author abstract modified)

198207 Anden, Nils-Erik. Department of Pharmacology, University of Goteborg, Fack, S-400 33 Goteborg 33, Sweden **Effects of oxotremorine and physostigmine on the turnover of dopamine in the corpus striatum and the limbic system.** Journal of Pharmacy and Pharmacology (London). 26(9):738-740, 1974.

The effects of oxotremorine and physostigmine on the homovanillic acid (HVA) concentrations in the rabbit corpus striatum and the limbic system were studied. Treatment with oxotremorine or physostigmine for 3 hours resulted in an increase in brain HVA of methylscopolamine pretreated rabbits. The physostigmine induced rises were between those seen after the two doses of oxotremorine. In all cases, the percentage increases were about the same in the corpus striatum and in the limbic system. After blockade of both peripheral and central muscarinic receptors by trihexyphenidyl, the effects of oxotremorine and physostigmine on HVA concentration in the corpus striatum were almost completely inhibited and the differences from the untreated controls were not significant. Increases in the limbic system were significantly reduced. Besides dopamine, the neostriatum and dopamine rich areas of the limbic system seem to contain high levels of acetylcholine, and further research is recommended on the interactions between dopamine and acetylcholine mechanisms in the various brain nuclei. 13 references.

198209 Christiansen, Jan; Squires, Richard F. Research Labortorties, A/S Ferrosan, Sydmarken 5, 2860 Soeborg, Denmark **Antagonistic effects of neuroleptics and apomorphine on synaptosomal tyrosine hydroxylase in vitro.** Journal of Pharmacy and Pharmacology (London). 26(9):742-743, 1974.

The antagonistic effects of nine neuroleptics and apomorphine on synaptosomal tyrosine hydroxylase of rat striatum in vitro were examined. Neuroleptics included spiramide, thioproperazine, perphenazine, alpha-fluphenazine, flupenthixol, chlorpromazine, thioridazine, clozapine, and beta-flupenthixol in order of decreasing antiapomorphine potency according to a 3H-H20 assay. A correlation between the in vitro activity of the compounds and their potency in vivo suggests that the postulated presynaptic dopamine receptors on synaptosomes are similar to postsynaptic dopamine receptors. 9 references.

198210 Bowers, Malcolm B., Jr.; Rozitis, Angelica. Department of Psychiatry, Yale University School of Medicine, 333 Cedar Street, New Haven, CT 06510 **Regional differences in homovanillic acid concentrations after acute and chronic administration of antipsychotic drugs.** Journal of Pharmacy and Pharmacology (London). 26(9):743-745, 1974.

Acute or chronic doses of chlorpromazine, thioridazine, clozapine, or fluphenazine enanthate were administered to rabbits and the effects of these treatments upon homovanillic acid (HVA) levels in three brain regions which contain dopamine were assessed. Findings suggest that the caudate nucleus of rabbits responds to chronic antipsychotic drug administration differently from limbic forebrain and hypothalamus. Another

treatment parameter was added whereby regional differences in effects upon dopamine metabolism after antipsychotic drugs may be observed and are consistent with the possibility that the clinical effects of these drugs may be manifestations of differential regional effects upon dopamine receptors. 9 references.

198211 Jori, A.; Caccia, S. Istituto di Ricerche farmacologiche "Mario Negri", Via Eritrea 62, Milan, Italy 20157 **Distribution of amphetamine and its hydroxylated metabolites in various areas of the rat brain.** Journal of Pharmacy and Pharmacology (London). 26(9):746-748, 1974.

A specific and sensitive gas chromatographic method was used to measure the relative concentrations of amphetamine and its hydroxylated metabolites in various areas of the rat brain at different times after a single dose of amphetamine. Amphetamine reached high levels in all areas studied, but seemed preferentially localized in the brainstem and hemispheres. Amphetamine disappeared rapidly from all areas, with no significant differences. The rate of disappearance of p-hydroxyamphetamine, formed from the parent compound mostly by liver metabolism, was slower than that of the amphetamine in all other areas examined. P-hydroxynorephedrine reached maximal levels at 5 h after dosage and accumulated in decreasing order in brainstem, hemispheres, cerebellum, and striatum. Its low concentration in the striatum is justified by the presence in this area of a large number of dopamine nerve endings lacking dopamine 3-hydroxylase, the enzyme responsible for the hydroxylation of p-hydroxyamphetamine to p-hydroxynorephedrine. Finally, the presence of large concentrations of p-hydroxynorephedrine in noradrenergic areas, such as the brainstem, is consistent with the hypothesis that it is retained in the noradrenaline nerve endings and is responsible for the amphetamine induced long lasting noradrenaline depletion. 13 references.

198223 Wauquier, A.; Niemegeers, C. J. E. Department of Pharmacology, Janssen Pharmaceutica, Research Laboratories, B-2340 Beerse, Belgium **Intracranial self-stimulation in rats as a function of various stimulus parameters: V. Influence of cocaine on medial forebrain bundle stimulation with monopolar electrodes.** Psychopharmacologia (Berlin). 38(3):201-210, 1974.

The effects of different subcutaneous doses of cocaine on self-stimulation in rats were studied. Six different stimulus parameter combinations (SPC's), inducing different predictable response rates were used. Cocaine showed a dose related response stimulation. Apomorphine, amphetamine and cocaine have some properties in common but there are also important differences. With the three compounds response stimulation is related to the total control response rates at the different SPC's and is the highest at the two SPC's inducing the lowest control response rate. The differences in response stimulation associated with low intensity and low frequency SPC's could be related to a different mechanism of action. The response depression, the highest with apomorphine and the lowest with cocaine seems to be related to the stereotype inducing property of the compounds. 18 references. (Author abstract)

198224 De Caro, G.; Micossi, L. G.; Venturi, F. Institute of Pharmacology and Pharmacognosy, Faculty of Pharmacy, University of Camerino, I-62032 Camerino, Italy **Behavioural and electrocortical modifications induced in the rat by intraventricular injection of physalaemin and eledoisin.** Psychopharmacologia (Berlin). 38(3):211-218, 1974.

The effects of intraventricular injection of eledoisin and physalaemin in the rat were studied. Both peptides reduced exploratory behavior; eledoisin, but not physalaemin, produced catatonia, reduction of muscular strength, tremor and sialorrhea. The electrocorticogram showed the signs of a depressive effect both after physalaemin and eledoisin administration. 8 references. (Author abstract)

198434 Darbinyan, T. M.; Golovchinsky, V. B.; Plekhotkina, S. I.; Bogdanov, K. Yu. A. V. Vishnevskogo AMN SSSR, Institute of Surgery imeni A. V. Vishnevskiy, Moscow /**A study of neurophysiological mechanisms of general anesthesia with ketamin.**/ Issledovaniye neyrofiziologicheskikh mekhanizmov obshchey anestizii ketaminom. Vestnik Adkademii Meditsinskikh Nauk SSSR (Moskva). No. 7:3-19, 1974.

The effect of ketamin on spontaneous and evoked electrical activity of various areas of the brain was studied in chronic and acute experiments on cats. Comparisons were made between the effect of ketamin on cats breathing spontaneously, and those subjected to artificial ventilation. Particular attention was devoted to the somatosensory, optic and associative zones of the cortex. Ketamin was found to markedly affect the activity of various cortical and subcortical structures, giving rise to slow waves with a frequency of 3 Hz and superimposed fast vacillations, but without any essential shifts in the evoked responses of the cortex and subcortex. The combination of electroencephalographic readings, small convulsive fits and the absence of a motor component of the convulsive activity was tentatively concluded to indicate that ketamin works as a general anesthesia by excitation of some diencephalic structures related to the maintenance of consciousness. 49 references. (Journal abstract modified)

198435 Kharkevich, D. A. Moscow Medical Institute imeni I. M. Sechenova, Moscow /**The influence of sodium oxybutyrate on interneuronal transmission of excitation at various levels of the central nervous system.**/ O vliyanii oksibutirata natriya na mezhneyronnuyu peredachu vozbuzhdeniya na raznykh urovnyakh tsentral0noy nervnoy sistemy. Vestnik Akademii Meditsinskikh Nauk SSSR (Moskva). No. 7:20-27, 1974.

The influence of sodium oxybutyrate on interneuronal transmission of excitation at the level of the spinal cord, medulla oblongata, cerebellum, pons Varolii, subcortical structure and cerebral cortex was studied. Experiments were conducted on narcoticized, curarized cats. Potentials elicited by various modes of stimulation of the sensory nerves were registered. Methods used included stimulation of the calf nerves, polysynaptic ducts; monosynaptic ducts, diaphragmatic nerves, pneumogastric nerves, and afferent ducts. Sodium oxybutyrate was found to characteristically suppress interneuronal transmission of excitation at all levels of the central nervous system. 19 references. (Journal abstract modified)

198436 Orlov, I. V.; Sherstnev, V. V.; Kravtsov, A. N. Moscow Medical Institute imeni I. M. Sechenova, Moscow /**On the specificity of neurochemical mechanisms dealing with nociceptive stimulation of neurons in various brain formations of rabbits.**/ O spetsifichnosti neyro-khimicheskikh mekhanizmov obrabotki bolevogo vozbuzhdeniya na neyronakh pazlichnykh obrazovaniy golovnogo mozga krolika. Vestnik Akademii Meditsinskikh Nauk SSSR (Moskva). No. 7:27-31, 1974.

The neurochemical mechanisms of pain integration on the cellular level were explored using phentanyl as an analgesic. Experiments on nondrugged and nonimmobilized rabbits demonstrate that both in intravenous administration and in microiontophoresis to individual neurons of the cerebral cortex, thalamus and reticular formation, phentanyl selectively and reversibly blocks long latent reactions of the activation

type or late activation components of nerve cell reactions to nociceptive stimulation. The block and restoration of responses to nociceptive stimulation developed parallel with a decrease in the sensitivity of the same neurons to microiontophoresis of acetyl choline, noradrenaline and glutamate. 15 references. (Journal abstract modified)

198481 Absava, G. I.; Markin, V. A. Laboratoriya farmakologii nervnoy sistemy, Instituta farmakologii AMN SSSR, Moscow **/On the influence of neuroleptics on the cortico-reticular system of the brain (histochemical and biochemical investigation)./** O vliyanii neyrolepticheskikh veshchestv na kortiko-retikulyarnuyu sistemu golovnogo mozga (gistokhimicheskoye i biokhimicheskoye issledovaniye). Farmakologiya i Toksikologiya (Moskva). 36(6):653-657, 1973.

Comparative histochemical and biochemical investigations were made of aminazine and triftazine influence on acidic enzyme activity and sodium, potassium and chlorine ions in the corticoreticular system of rats' brains to determine how neuroleptics affect functional reciprocity between various levels of the corticoreticular system. For histochemical study, the activity of flavine and NAD dependent dehydrogenases was measured. For the biological study, potassium and sodium ionic content was determined by the flame-photometric method. Chloride content was measured by the retroactive conductor-metric titration of surplus nitrate by sulphocynate ammonia. Aminazine was found to retard activity of dehydrogenases in the sincipital cortex and reticular formation of the middle brain, whereas triftazine did not. Aminazine increased potassium and chlorine content and decreased sodium content in the cortex and increased sodium content in the middle brain. Triftazine decreased content of potassium, sodium and chlorine in the cortex and the middle brain. 18 references. (Journal abstract modified)

198485 Glushchenko, T. S. Laboratoriya funktsional0noy neyrokhimii, Institut fiziologii im. I. P. Pavlova, AN SSSR, Leningrad **/Proteinase activity of different sections of the brain during corazol (pentylenetetrazol) induced convulsions./** Proteinaznaya aktivnost0 razlichnykh otdelov golovnogo mozga pri korazolovykh sudorogakh. Farmakologiya i Toksikologiya (Moskva). 36(6):677-680, 1973.

Proteinase activity in the brain during and immediately following corazol (pentylenetetrazol) induced convulsions was studied in rats. Introduction of corazol produced convulsions lasting 12 to 15 minutes. Twenty minutes after injection, activation of neutral proteinases occurred in the mesencephalon and in the large hemispheres of the brain, while acid proteinases were inhibited in the large hemispheres and the cerebellum. Two hours thereafter, neutral proteinase activity increased in the aforementioned spheres, while acid proteinase activity continued to decrease. After 6 hours, some decline of neutral proteinase activity was observed in the midbrain, accompanied by a greater decline in the large hemispheres and normalization in the cerebellum. Acid proteinase activity returned to normal in the cerebellum, and close to normal in the large hemispheres. The pentylenetetrazol induced convulsions had no effect on the activity of acid proteinases in the mesencephalon. 10 references. (Journal abstract modified)

198486 Samoylova, Z. T.; Tret0yakova, K. A.; Khalyutina, L. V. Tsentral0nyy institut usovershenstvovaniya vrachey, Moscow **/The effect of L-DOPA on the development of reserpine induced parkinsonism and catecholamine metabolism in rats./** Vliyaniye L-DOPA na razvitiye rezerpinovogo parkinsonizma i obmen katekholaminov u krys. Farmakologiya i Toksikologiya (Moskva). 36(6):684-687, 1973.

The influence of L-DOPA on experimentally induced parkinsonism was studied in albino male rats. Considering that interruption of dopamine exchange in the brain is an important pathogenetic link in the development of parkinsonism, the content of catecholamine in the brain was noted and isolated from the urine. Other areas of investigation included: behavior and motor activity; appearance of tremors; changes in gait; and the vegetative functions of respiration, bodyweight and distrophic changes in the skin. Catecholamine level in the brains of rats suffering from parkinsonism was found to be lower than normal. Administration of L-Dopa raised the dopamine content in the brain, and intensified passage of dopamine, norepinephrine and epinephrine with urinary excretion. L-DOPA exerted an inhibitory influence on the development of reserpine induced parkinsonism, prolonged the ailing animals' lives, and raised the level of motor activity. 1 reference. (Journal abstract modified)

198606 Holtzman, Stephen G. Emory University, Department of Pharmacology, Atlanta, GA 30322 **Interactions of pentazocine and naloxone on the monoamine content of discrete regions of the rat brain.** Biochemical Pharmacology (Oxford). 23(21):3029-3035, 1974.

The effects of pentazocine on the norepinephrine (NE), dopamine (DA), and serotonin (5-HT) content of discrete regions of the rat brain were investigated alone and after pretreatment with naloxone. Pentazocine, 5.6to 56mg/kg, caused dose related decreases in the catecholamine content of these regions. NE levels were lowered in all brain regions, whereas the depletion of DA was restricted to the cortex and striatum. The 5-HT levels were relatively unaffected by pentazocine. Pretreatment with naloxone antagonized pentazocine induced depletion of brain DA. It also blocked the pentazocine induced depletion of NE in the cortex and midbrain, but did not affect depletion of NE in the medulla and actually enhanced the depletion of hypothalamic NE. A significant depletion of medullary 5-HT was observed only in rats pretreated with naloxone. Findings are consistent with the concept that pentazocine's agonistic spectrum of activity involves two components, one which is blocked by naloxone and one which is not. 19 references. (Author abstract modified)

198613 Edmonds, Harvey L.; Stark, Larry G.; Hollinger, Mannfred A. Department of Pharmacology, School of Medicine, University of California, Davis, CA 95616 **The effects of diphenylhydantoin, phenobarbital, and diazepam on the penicillin-induced epileptogenic focus in the rat.** Experimental Neurology. 45(2):377-386, 1974.

Techniques are described for the injection of minute quantities of penicillin into discrete intracortical loci in freely moving rats. The time course and quanitification of the penicillin induced cortical afterdischarges and seizure activity were determined. The compound 14C-penicillin was used to test assumptions related to the spread of this agent from the intracortical site of injection, and the degree of spread was limited to the ipsilateral hemisphere along cortical surface and was verified by both scintillation counting and autoradiography. The effects of diphenylhydantoin, phenobarbital and diazepam on the penicillin induced focal seizures were not marked. None of the agents produced a significant decrease in spiking activity, number of afterdischarges, total amount of afterdischarge activity or average length of afterdischarge, even though the higher doses of all three compounds produced signs of neurotoxicity. 13 references. (Author abstract modified)

198835 Arushanyan, E. B.; Belozertsev, Yu. A.; Ayvazov, K. G. Medical Institute, Chita, USSR /**Comparative effect of phenamine (amphetamine) and caffeine on the background activity of cortical sensorimotor neurons and their reactions during stimulation of the caudate nucleus.**/ Sravnitel0noye vliyaniye fenamina i kofeina na fonovuyu aktivnost0 sensomotornykh neyronov kory i ikh otvety pri razdrazhenii khovostatogo yadra. Byulleten0 Eksperimental0noy Biologii i Meditsiny (Moskva). 8(7):59-62, 1974.

The effects of amphetamines and caffeine on the background activity of the sensorimotor neurons of the cortex and their responses to stimulation of the caudate nucleus were compared in cats. With low frequency stimulation of the caudate nucleus, amphetamine (1mg/kg) and caffeine (20mg/kg) did not greatly affect the frequency of background activity but increased the number of spontaneously active units in the cortex. Amphetamine depressed the inhibition of the caudate nucleus originating in the ventrolateral portion of the head more than that originating in the dorsomedial portion. Localization of the stimulating electrodes was not essential for the action of caffeine. 10 references. (Author abstract modified)

199210 Nakanishi, M.; Setoguchi, M. Research Laboratories of Yoshitomi Pharmaceutical Industries Ltd., 955 Koiwai, Yoshitomi-cho, Chikujo-Gun, Fukuoka-Ken, Japan **Studies on psychotropic drugs: XVII. Effects of 3-chloro-5-(3-(4-piperidino-4-carbamoyl-piperidino)-propyl)-10,11-dihydro-5(H)-dibenz(b,f)azepine dihydrochloride monohydrate (Y-4153) on the metabolism of biogenic amines.** Arzneimittel-Forschung (Aulendorf). 23(6):806-810, 1973.

The pharmacological properties of 3-chloro-5-(3-(4-piperidino-4- carbamoyl-piperidino)-propyl)-10,11-dihydro-5(H)-dibenz-(b,f)-azepine dihydrochloride monohydrate (Y-4153) were studied. It was found that Y-4153 inhibited the uptake of serotonin (5-HT), norepinephrine (NE) and dopamine (DA) into rat platelet in in vitro condition. Its inhibitory potency for 5-HT uptake was weaker than that of imipramine (IMP) but stronger than that of chlorpromazine (CPZ). The effects of each test compound administered twice, on the amine levels of the rat brain were examined, and it was found that IMP increased the endogenous level of 5-HT and CPZ decreased that of NE, whereas no significant change was observed with Y-4153. The results obtained in this study thus suggest that the pharmacological properties of Y-4153, though coming in between when compared with those of IMP and of CPZ, bear more resemblance to those of CPZ and the mode of action of Y-4153 is to be found in increasing the turnover of catecholamines in the adrenergic neuron in the central nervous system. 28 references. (Author abstract modified)

199277 Blosser, J. C.; Catravas, G. N. Armed Forces Radiobiology Research Institute, Bethesda, MD 20014 **Action of reserpine in morphine-tolerant rats: absence of an antagonism of catecholamine depletion.** Journal of Pharmacology and Experimental Therapeutics. 191(2):284-289, 1974.

The mechanism of resistance to the catecholamine depleting effects of reserpine in morphine tolerant rats was examined. In vitro, morphine did not alter reserpine inhibition of 3H-norepinephrine uptake by synaptic vesicles. Uptake by vesicles isolated from morphine tolerant animals was as susceptible to reserpine inhibition as that of corresponding preparations from salir.e treated controls. Intraperitoneally administered reserpine only partially reduced brain catecholamine levels in most rats treated chronically with morphine. Reserpine injected intravenously depleted norepinephrine and dopamine in experimental animals to the same extent as controls treated by either route of administration. Animals chronically treated with morphine and with only partially reduced norepinephrine concentrations exhibited tritium levels less than 50% those of controls. It is concluded that an increased resistance to reserpine cannot be correlated with central nervous system tolerance to morphine. Systematic inactivation of reserpine may be enhanced as a result of chronic morphine treatment. 13 references. (Author abstract modified)

199347 Yang, Y.-Y. T.; Neff, N. H. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **N-acetyltransferase of brain: possible involvement in the metabolism of the biogenic amines. (Unpublished paper).** Washington, D. C., NIMH, 17 p.

The distribution and properties of N-acetyltransferase were investigated with rats. N-acetyltransferase of rat brain is active toward a wide variety of naturally occurring biogenic amines as well as amphetamine. The Km value for indolethylamines is lower than for phenylethylamines. The enzyme requires a divalent metal ion and the activity is inhibited by harmaline but not by pargyline. After dialysis of the crude homogenate of various parts of the brain, activity is increased and rather evenly distributed. It is suggested that the enzyme may play a role in the metabolism of the biogenic amines of brain, especially after drugs that block monoamine oxidase. 15 references. (Author abstract modified)

199443 Serkov, F. N.; Yanovsky, E. Sh.; Tal0nov, A. N. Institut Fiziologii im. A. A. Bogomol0tsa AN USSR, Kiev /**The influence of nembutal, chloralose and urethane on inhibitory postsynaptic potentials of cortical neurons.**/ Vliyaniye nembultala, khloralozy i uretana na tormozyashchiye postsinapticheskiye potentsialy korkovykh neyronov. Neyrofiziologiya (Kiev). 6(4):339-349, 1974.

The effect of nembutal, chloralose and urethane on inhibitory postsynaptive potentials, IPSPs, in the auditory cortical neurons produced by stimulation of geniculocortical fibers was studied in cats immobilized by d-tubocurarine. The duration of IPSPs nearly doubled after nembutal administration, but the latencies were shortened. Chloralose raised the relative quantity of evoked postsynaptic potential-spike-IPSP type reactions and caused a three to fourfold increase in IPSP duration. The latent period of IPSP was reduced. Urethane decreased IPSP duration to 30 milliseconds. About 2% of the neurons studied before drug application possessed IPSP latencies ranging from 1.0to 1.5milliseconds. After drug injection, the relative quantity of IPSP latencies rose to 5.7%. Such IPSPs were assumed to be monosynaptical. The mechanism of the narcotics' action on the inhibitory system of the cerebral cortex was also briefly discussed. 22 references. (Journal abstract modified)

199622 Fjalland, B. Department of Pharmacology and Tocicology, H. Lundbeck and Co. A/S, Ottiliavej 7-9, DK-2500 Valby, Denmark **Sympathomimetic amines and gastric secretion in rats.** Acta Pharmacologica et Toxicologica (Copenhagen). 35(4):293-299, 1974.

The influence of amphetamine, apomorphine and methylphenidate on basal gastric secretion was investigated using fistula and pylorus ligated rats. The antisecretory effect of amphetamine was reversed by pretreating the animals with alpha-methyl-p-tyrosine (alpha-MT). The decreased output following methylphenidate in shay rats was reduced by an alpha-MT treatment, but alpha-MT was not able to antagonize the antisecretory effect of methylphenidate in fistula rats. Apomorphine exhibited antisecretory properties in fistula rats

and gastric stimulating effects in shay rats, the latter effect being reversed by alpha-MT treatment. The results obtained indicate that the antisecretory effects of amphetamine and methylphenidate may be due to their amine releasing properties. 13 references. (Author abstract)

199623 Thomsen, Klaus; Jensen, Jorgen; Olesen, O. Vendelin. Psychopharmacology Research Unit, Aarhus University Psychiatric Institute, DK-8240 Risskov, Denmark **Lithium-induced loss of body sodium and the development of severe intoxication in rats.** Acta Pharmacologica et Toxicologica (Copenhagen). 35(4):337-346, 1974.

Four groups of rats were given food containing 0, 40, 70, or 100 mmol lithium chloride per kg dry weight, respectively, in a study of lithium induced loss of body sodium and the development of severe intoxication. They had free access to water and to NaCl. This regimen was maintained for 1 month, and the rats did not develop lithium intoxication in spite of the high lithium dosage. The rats given lithium containing food drank more sodium chloride solution than the control rats, and the intake increased with the lithium content of the food. In the two groups given the highest lithium dosages, discontinuance of access to the sodium chloride solution led within 4 days to a marked loss of body sodium and a proportionate loss of bodyweight, a significant decrease of serum sodium, and the development of severe lithium intoxication. Bodyweight was reestablished by additional sodium chloride solution. The experiments indicate that administration of lithium leads to a lowered ability of the kidneys to conserve sodium and a consequent increased requirement for sodium. 12 references. (Author abstract modified)

199763 Dahl, Eva; Gjerstad, Leif I.; Skrede, Knut Kr. Institute of Neurophysiology, University of Oslo, Karl Johansgt. 47, Oslo 1, Norway **Persistent thalamic and cortical barbiturate spindle activity after ablation of the orbital cortex in cats.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 33(5):485-496, 1972.

The orbital cortex was ablated in barbiturate anesthetized cats in order to investigate a possible role of this part of the brain in the generation of spontaneous thalamic and cortical rhythmic discharges. Spindles recorded from the lateral, the suprasylvian and the ectosylvian cortices were generally in all respects unaffected by orbital ablations. Spindles recorded near the lesion often showed a reduced amplitude while the other parameters were unchanged. Following orbital lesions the potentials evoked in the postcruciate cortices by stimulation of peripheral nerves decreased in parallel with the amplitude of the spindles recorded from the same areas. Evoked potentials of the ventral postero-lateral (VPL) nucleus were unaffected by the lesions. The findings are in accordance with the hypothesis that rhythmic barbiturate activity is generated in the thalamus and transmitted to the cortex by the specific thalamic relay cells. 23 references. (Author abstract modifed)

199764 Wada, J. A.; Balzamo, E.; Meldrum, B. S.; Naquet, R. Faculty of Medicine, University of British Columbia, Vancouver, Bristish Columbia, Canada **Behavioural and electrographic effects of L-5-hydroxytryptophan and D,L-parachlorophenylalanine on epileptic Senegalese baboon (Papio papio).** Electroencephalography and Clinical Neurophysiology (Amsterdam). 33(5):520-526, 1972.

In the Senegalese baboon Papio papio, the behavioral and electrographic effects of the serotonin precursor, L-5-hydroxytryptophan (5-HTP) and a serotonin depletor, D,L-parachlorophenylalanine (pCPA) were examined with special attention to the preexisting photosensitivity and epileptiform electrographic activity. L-5-HTP depressed motor and EEG responses to photic stimulation for 1-4 h after injection; 48 h after D,L-pCPA, myoclonic responses to photic stimulation were enhanced. Consistent reduction of photosensitivity was observed 4-7 days after pCPA. Both drugs activated spontaneous epileptiform electrographic abnormalities. These changes in background activity were often chronologically independent of the changes in photically induced responses. It is suggested that serotonergic systems can play a role in the photomyoclonic syndrome in Papio papio. 34 references. (Author abstract)

199765 Rose, Guenter H.; Gruenau, Steven P.; Spencer, John W. Department of Psychiatry, Mental Retardation Program, Neuropsychiatric Institute, University of California, Los Angeles, CA 90024 **Maturation of visual electrocortical responses in unanesthetized kittens: effects of barbiturate anesthesia.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 33(2):141-158, 1972.

The development of visual electrocortical responses (VERs) evoked by brief, focused light flashes were studied in unanesthetized kittens. Immobilized with Flaxedil between birth and 5 weeks of age. The maturational sequence of the VER in the unanesthetized kitten in the first 2 postnatal weeks consists of a long latency negative (N2) wave at 2-4 days of age, a double negative wave form (N1 - N2) at 5-8 days of age, and a positive-negative-negative VER (P1N1N2) between 9-14 days of age. This sequence is virtually identical to that obtained under barbiturate anesthesia. Beyond 2 weeks old the principal VER alterations in unanesthetized kittens consist of the temporary appearance of a negative component (NA) between the N1 and N2 waves, and a positive component (P2) preceding the N2 wave, resulting in an adultlike, variable P1N1P2N2 complex by 30 days of age. Pentobarbital anesthesia acts to increase the amplitude of the P1N1 components while subsequently reducing or eliminating the latter components, which results in a biphasic P1N1 wave form by 30 days of age. The relationship of these findings to other indexes of maturation in the kitten as well as their relevance to future developmental psychobiological studies are stressed. 61 references. (Author abstract modified)

199769 Reiffenstein, R. J.; Triggle, Cecile. Department of Pharmacology, University of Alberta, Edmonton 7, Alberta, Canada **Sensitivity of denervated cerebral cortex to cholinomimetics.** Electoencephalography and Clinical Neurophysiology (Amsterdam). 33(2):215-220, 1973.

The sensitivity of denervated cerebral cortex to cholinomimetics was examined. Chronically denervated slabs of cerebral cortex are not supersensitive to cholinomimetics which are not broken down by cholinesterase. Thus chronic slabs do not show denervation supersensitivity, at least as it occurs in the peripheral nervous system. Cholinoceptive function is not required for seizure maintenance in chronic slabs since atropine does not block the prolonged seizures of chronic slabs. Cholinomimetics reduce the number of detectable active cells at all depths in the cortex in both acute and chronic slabs. Cells firing during cholinomimetic induced seizures have the same depth distribution pattern as spontaneously active neurons, both in acute and chronic slabs. 26 references. (Author abstract)

199770 Schnell, R. C. Department of Pharmacology and Toxicology, School of Pharmacy, Purdue University, West Lafayette, IN 47907 **Enhancement of the chlorpromazine-in-**

duced suppression of the conditioned avoidance response by carbonic anhydrase inhibition. Neuropharmacology (Oxford). 13(9):847-850, 1974.

The influence of carbonic anhydrase inhibition upon the chlorpromazine induced suppression of a conditioned avoidance response (CAR) was examined in the rat. Suppression of a conditioned avoidance response in rats by chlorpromazine HCl (CPZ) was enhanced (230%) after treatment with acetazolamide. This enhanced pharmacological response in the acetazolamide treated rats was accompanied by increased brain levels of 35S after administration of chlorpromazine. In parallel experiments, an analogue of chlorpromazine, CL-13,850, which possess no carbonic anhydrase inhibitory activity, had no influence on the pharmacological effect on the brain levels of 35S after administration of chlorpromazine. The data suggest the enhanced pharmacological response following acetazolamide treatment is the result of increased brain levels of chlorpromazine brought about by carbonic anhydrase inhibition. 16 references. (Author abstract)

199771 Palmer, G. C.; Manian, A. A. Department of Pharmacology, University of New Mexico School of Medicine, 915 Stanford NE, Albuquerque, NM 87131 **Modification of the receptor component of adenylate cyclase in the rat brain by phenothiazine derivatives.** Neuropharmacology (Oxford). 13(9):851-866, 1974.

The manner in which several derivatives of phenothiazines modify the postulated receptor component of the adenylate cyclase enzyme in the rat brain was examined. Incubated tissue slices from rat cerebral cortex and medial and lateral hypothalamus readily accumulated cyclic adenosine 30,50-monophosphate (cyclic-AMP) in response to added norepinephrine (NE). The monohydroxylated derivatives of chlorpromazine (CPZ), prochlorperazine, perphenazine, promazine and fluphenazine and respective parent compounds including promethazine and thiothixene were the most potent inhibitors of the stimulation of cyclic-AMP by NE. The NE induced cyclic-AMP response in the medial hypothalamus was more sensitive to inhibition by these pharmacologically active phenothiazines. The results suggest that antiadrenergic actions of pharmacologically active phenothiazines may be manifested at the receptor component of adenylate cyclase. 46 references. (Author abstract modified)

199772 Wolfarth, S.; Dulska, E.; Lacki, M. Department of Pharmacology, Polish Academy of Sciences, 31-344 Krakow, Poland **Comparison of the effects of the intranigral injections of cholinomimetics with systemic injections of the dopamine receptor stimulating and blocking agents in the rabbit.** Neuropharmacology (Oxford). 13(9):867-875, 1974.

The effects of intranigral injections of cholinomimetics, acetylcholine, methacholine and neostigmine were examined in the rabbit. The cholinergic stimulation of the substantia nigra of the rabbit, induced by intranigral injections of acetylcholine, methacholine or neostigmine, produced behavioral and electroencephalogram (EEG) alerting, various forms of stereotyped behavior and autonomic symptoms, followed by a preepileptic EEG pattern (sharp waves, spike and waves, and multispike complexes) and an epileptic EEG pattern accompanied in most of cases by clonico tonic convulsions. The effects of cholinomimetics were abolished by intranigral injections of atropine, or by subcutaneous injections of spiroperidol. The catalepsy produced by spiroperidol was abolished by intranigral neostigmine injections. The relationship between the cholinergic stimulation of the nigra and dopaminergic stimulation of the striatum is discussed. 30 references. (Author abstract modified)

199773 Ladisich, W. Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse- 10, D-8000 Munchen 40, Germany **Effect of progesterone on regional 5-hydroxytryptamine metabolism in the rat brain.** Neuropharmacology (Oxfrod). 13(9):877-883, 1974.

The influence of progesterone upon 5-hydroxytryptamine (5-HT) metabolism in the rat brain was investigated in view of a possible connection with premenstrual tension and postpartum depression. A progesterone dose, resulting in a plasma level which was still in a physiological range, increased 5-HT turnover in septum, hypothalamus and raphe. A higher unphysiological dose, besides producing a further increase of 5-HT turnover, also resulted in a decrease of 5-hydroxyindoleacetic acid (5-HIAA) levels which was most pronounced in the septum. Neither of the two doses showed a clearcut influence on 5-HT concentrations in any of the investigated brain areas. 14 references. (Author abstract)

199783 Peters, D. A. V. Department of Pharmacology, Faculty of Medicine, University of Ottawa, Ottawa, Canada **Chronic lysergic acid diethylamide administration and serotonin turnover in various regions of rat brain.** Journal of Neurochemistry (Oxford). 23(4):625-628, 1974.

The effects of chronic lysergic acid diethylamide (LSD) treatment on different areas of rat brain were examined. Acute injections of LSD to rats resulted in evidence of a reduced 5-hydroxytryptamine (5-HT) turnover in all brain areas studied. In contrast, a much smaller dose of LSD repeated daily for 1 month produced a significantly reduced turnover only in the midbrain area. The pons/medulla and forebrain areas showed small and not statistically significant increases in 5-HT turnover. 20 references. (Author abstract)

199785 Gey, K. F.; Georgi, H. Department of Experimental Medicine, F. Hoffmann-La Roche & Co. Ltd., Basel, Switzerland **Effect of neurotropic agents on total pyridoxal phosphate and on the activity of the decarboxylase of aromatic amino acids as well as of other pyridoxal phosphate-dependent enzymes in rat brain.** Journal of Neurochemistry (Oxford). 23(4):725-738, 1974.

Rats received single intraperitoneal injections of various neuroactive chemicals in order to compare the changes of gross behavior and the level of pyridoxal phosphate as well as the activity of the decarboxylase of aromatic amino acids, of glutamate decarboxylase and of tyrosine transaminase in the brain. The majority of excitatory agents tested (i.e. convulsive like amino-oxyacetate, thiosemicarbazide, pentylenetetrazol and oxotremorine; stimulants such as amphetamine, theophylline and methylphenidate; the amphetamine like monoamine oxidase inhibitor tranylcypromine as well as the classical monoamine oxidase inhibitor iproniazid when combined with the monoamine releaser Ro 4-1284 caused a decrease in aromatic decarboxylase activity which was coexistent with maximal changes of gross behavior and partly preceded the latter. Depression of obvious central nervous functions was almost regularly accompanied and in part preceded by increase of DCA activity. The activity of glutamate decarboxylase was significantly reduced by thiosemicarbazide only, whereas a distinct increase in enzyme activity was exclusively observed after atropine. Tyrosine transaminase activity was significantly diminished by amino oxyacetate only and showed a late increase after tranylcypromine. It is concluded that there is an inverse relationship, in the majority of neuroactive chemicals tested, between changes of gross behavior and cerebral aromatic decarboxylase activity. 56 references. (Author abstract modified)

199788 Baldessarini, R. J.; Yorke, C. Psychiatric Research Laboratories, Massachusetts General Hospital, Boston, MA 02114 **Uptake and release of possible false transmitter amino acids by rat brain tissue.** Journal of Neurochemistry (Oxford). 23(4):839-848, 1974.

The uptake and release of possible false transmitter amino acids by rat brain tissue were studied. The uptake of L[14C]glutamine by a crude isolated nerve ending fraction of rat brain was found to be linear with time for at least 5 min, profoundly temperature dependent, apparently half saturated at a substrate concentration of 0.26 mM, partially inhibited by dinitrophenol and ouabain and elevated [K+], weakly Na+ dependent, poorly inhibited by drugs which block uptake of biogenic amines and more strongly inhibited by glutamic acid than by aspartic acid, gamma-aminobutyric acid, glycine or methionine. The [14C]glutamine taken up appeared to be associated with nerve endings and was released by membrane disruption; about 20% was associated with free mitochondria. [14C]glutamine was not released by unlabeled glutamate or several aromatic amines. It is concluded that the neuropsychiatric features of porphyria are not likely due to a false transmitter role for aminolevulinic acid although such a role for glutamine in hepatic encephalopathy or other neuropsychiatric diseases should be considered. 43 references. (Author abstract modified)

199805 Chippendale, Thomas J.; Cotman, Carl W.; Kozar, Mark D.; Lynch, Gary S. Department of Psychology, Princeton University, Princeton, NJ 08540 **Analysis of acetylcholinesterase synthesis and transport in the rat hippocampus: recovery of acetylcholinesterase activity in the septum and hippocampus after administration of diisopropylfluorophosphate.** Brain Research (Amsterdam). 81(3):485-496, 1974.

The site and rate of synthesis, as well as the transport dynamics, of newly synthesized acetylcholinesterase (AChE) was studied in the septum and hippocampus of the rat. Histochemical and biochemical techniques were employed to study time dependent changes in AChE activity of the medial septal nucleus and hippocampus following systemic administration of the anticholinesterase diisopropylfluorophosphate. In both septum and hippocampus, an initially rapid phase of recovery was followed by a slower recovery with similar rate constants for the two regions. Analysis of AChE synthesis in the septo-hippocampal system revealed that recovery of activity in the septum preceded that in the hippocampus. The data suggest that the bulk of septal AChE in the hippocampus is transported via the slow component of axoplasmic flow. A fast component may exist, but the experimental arrangement did not permit the clear demonstration of any rapid axoplasmic flow. 35 references. (Author abstract)

199807 Yoshimura, H.; Fujiwara, M.; Ueki, S. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka, Japan **Biochemical correlates in mouse-killing behavior of the rat brain: brain acetylcholine and acetylcholinesterase after administration of delta9-tetrahydrocannabinol.** Brain Research (Amsterdam). 81(3):567-570, 1974.

In a study of the biochemical correlates of mouse killing behavior in the rat, brain acetylcholine (ACh) and acetylcholinesterase (AChE) after the administration of delta9-tetrahydrocannabinol (THC) were measured. One hour after a single injection of THC, 60% of the rats showed mouse killing behavior. ACh levels of the striatum and amygdala in both killer and nonkiller rats of the THC treated groups were significantly higher than in the control group. There was no significant difference in ACh levels of all brain areas between the killer and nonkiller rats of the THC treated group. The activity of AChE in all brain areas, including the striatum and amygdala which showed higher ACh levels as mentioned above, was unchanged after THC as compared with the control values. There was no significant difference between the killer and nonkiller rats. It is suggested that mouse killing behavior induced by THC is not mediated through the cholinergic system in the brain and may be somehow different in mechanism from that in either spontaneous or olfactory bulbectomized killer rats. 23 references.

199811 Chou, Dorothy T.; Lee, H. K.; Wang, S. C. Department of Pharmacology, Columbia University, New York, NY 10032 **Locus of central depressant action of flunitrazepam.** Experimental Neurology. 45(3):509-519, 1974.

The dose response relationship for depressant action of flunitrazepam on contralateral extensor reflexes was studied in midcollicular decerebrate and acute spinal cats. The reflex response was more sensitive to the depression of the drug in midcollicular than in acute spinal preparations. The stimulation experiments showed that this drug also depressed the facilitation and inhibition of the knee jerk produced by activating the brainstem reticular system. The dose response curve of the effects of this drug on mesencephalic reticular and spinal internuncial neuronal activity revealed that depression occurred at both levels. These findings suggest that the higher potency of flunitrazepam is attributable not only to its highly potent depressant action on the mesencephalic reticular system but also to its substantial depressant action on the spinal interneurons. 12 references. (Author abstract modified)

199861 Johnson, Dennis D.; Lowndes, Herbert E. Department of Pharmacology, College of Medicine, University of Saskatchewan, Saskatoon, Canada **Reduction by diazepam of repetitive electrical activity and toxicity resulting from soman.** European Journal of Pharmacology (Amsterdam). 28(2):245-250, 1974.

The reduction by diazepam of repetitive electrical activity and toxicity resulting from soman was reported. The organophosphate cholinesterase inhibitor soman (methyl pinacolylphosphonofluoridate) produces potentiation of twitch tension in rat anterior tibial and phrenic nerve-diaphragm preparations by initiating repetitive electrical activity in the vicinity of the motor nerve terminals. Diazepam abolished this repetitive electrical activity and hence the associated potentiation of muscle twitch tension. These effects are produced by concentrations of diazepam that are without other apparent effects on neuromuscular transmission, as indicated by the absence of effect on normal twitch responses. The combination of diazepam with atropine provides additional protection against soman toxicity in rabbits. 25 references. (Author abstract)

199862 O'Donnell, Stella R.; Saar, Nili. Department of Physiology, University of Queensland, St. Lucia, 4067 Brisbane, Queensland, Australia **The effects of 6-hydroxydopamine and guanethidine on peripheral adrenergic nerves in the guinea pig.** European Journal of Pharmacology (Amsterdam). 28(2):251-256, 1974.

The effects of 6-hydroxydopamine and guanethidine on peripheral adrenergic nerves in the guinea pig were examined. Chemical sympathectomy was achieved in guinea pig trachea 24 hr after a single dose of 50mg/kg 6-hydroxydopamine (6-OHDA). This was shown by the disappearance of fluorescent nerve terminals, decreased uptake with retention of radioac-

tivity following incubation in (-)-3H-noradrenaline (50 nM) and the supersensitive response of the isolated tracheal chain preparation to noradrenaline. The susceptibility of the adrenergic nerve terminals in the lung to 6-OHDA resembled that of trachea, in that complete disappearence of fluorescent nerve terminals was achieved with the above doses, whereas doses higher than 100mg/kg were required to produce this in heart and iris. Chronic treatment of guinea pigs with guanethidine did not produce destruction of adrenergic nerves in peripheral tissues. 9 references. (Author abstract)

199863 Deitchman, David; Gomoll, Allen W.; Snyder, Robert W. Department of Pharmacology, Mead Johnson Research Center, Evansville, IN 47721 **Inhibition of sympathetic activity following chronic administration of 2-amino-4-(3,4-dichlorophenyl)-2-imidazoline (MJ 10459-2).** European Journal of Pharmacology (Amsterdam). 28(2):257-265, 1974.

The inhibition of sympathetic activity following chronic administration of 2-amino-4-(3,4-dichlorophenyl)-2-imidazoline (MJ 10459-2) was reported. MJ 10459-2 caused a prolonged reduction in sympathetic function demonstrable by depressed responses to direct, indirect, or reflex activation of the sympathetic nervous system. Direct increases in forelimb perfusion pressure, heartrate and contractile force, and nictitating membrane tension elicited by the appropriate neural stimulation were attenuated following chronic drug administration. Indirectly MJ 10459-2 decreased the pressor and positive cardiac responses to tyramine. Reflex increases in blood pressure and heartrate initiated by bilateral carotid occlusion were depressed by treatment. Diminished responses to sympathetic activation occurred coincidentally with enhanced responses to exogenously administered norepinephrine. The results suggest that MJ 10459-2 may elicit its previously observed antihypertensive action via a mechanism of reduced sympathetic function, probably resulting from depletion of endogenous norepinephrine. 10 references. (Author abstract modified)

199867 Karobath, Manfred E. Department of Experimental Psychiatry, Psychiatrische Universitatsklinik, University of Vienna, Vienna, Austria **Amantadine and D-145, an amantadine derivative, do not effect dopamine sensitive adenylate cyclase from the caudate-putamen of the rat brain.** European Journal of Pharmacology (Amsterdam). 28(2):376-378, 1974.

The effects of amantadine and D-145 amantadine derivative, on dopamine stimulated adenylate cyclase--an enzyme, which has been suggested to closely resemble the dopamine receptor in the central nervous system, have been examined. Homogenates of the caudate-putamen of the rat brain were used. Both drugs were ineffective, since they neither mimicked nor antagonized the action of dopamine on this enzyme. 9 references. (Author abstract)

199868 Palfreyman, Michael G.; Palfreyman, Elizabeth S.; Clark, Michael S. G. Beecham Research Laboratories, Medicinal Research Centre, 4th Avenue, Harlow, Essex, England **Effects of benapryzine, a new antiparkinson drug, on dopamine uptake into corpus striatum.** European Journal of Pharmacology (Amsterdam). 28(2):379-383, 1974.

The effects of benapryzine, a new antiparkinson drug, on dopamine uptake into corpus striatum were studied. The compound has little effect on noradrenaline uptake into the hypothalamus. Uptake inhibition is noncompetitive in both the striatum and hypothalamus. In contrast, benzhexol is a competitive inhibitor of noradrenaline uptake in the hypothalamus. 8 references. (Author abstract)

199869 Gutman, Yehuda; Boonyaviroj, Punya. Department of Pharmacology, School of Medicine, Jerusalem, Israel **Suppression by noradrenaline of catecholamine secretion from adrenal medulla.** European Journal of Pharmacology (Amsterdam). 28(2):384-386, 1974.

The suppression by noradrenaline of catecholamine secretion from adrenal medulla was reported. The release of catecholamines from the rat adrenal medulla caused by insulin hypoglycemia was blocked by noradrenaline without affecting hypoglycemia. It is suggested that release of catecholamines from the adrenal cells may be regulated by alpha-adrenoceptors, similar to the mechanism described for adrenergic nerve endings. 10 references. (Author abstract)

199870 Basuray, Biswa N.; Dutta, Samarendra N. Department of Pharmacology, Howard University, College of Medicine, Washington, DC 20001 **Effects of lithium chloride on cardiovascular responses induced by cholinergic and adrenergic stimulations.** European Journal of Pharmacology (Amsterdam). 28(2):387-390, 1974.

The effects of lithium chloride on cardiovascular responses induced by cholinergic and adrenergic stimulations were studied. Right vagus nerve of pentobarbital anesthetized rabbits was stimulated at different voltages after infusion of normal saline and of lithium chloride solution in distilled water. Lithium chloride infusion at a rate of 0.25mEq/0.25ml/min for 30 min decreased the effects of vagal stimulation on blood pressure and heartrate significantly when compared to those following saline infusion. Lithium chloride also decreased the effects of exogenous acetylcholine. Lithium failed to modify the effects of either cardiac accelerator nerve stimulation or of injection of norepinephrine. 13 references. (Author abstract)

199897 Blumenkrantz, N.; Asboe-Hansen, G. Department of Dermatology, University of Copenhagen, Rigshospitalet, Blegdamsvej, DK-2100 Copenhagen, Denmark **Reaction of cationic groups of chlorpromazine with anionic macromolecules: complexes with DNA, RNA, hyaluronic acid and heparin.** Acta Pharmacologica et Toxicologica (Kobenhavn). 34(1):27-32, 1974.

In vitro, chlorpromazine forms complexes with deoxyribonucleic acid, ribonucleic acid, hyaluronic acid and heparin. Irradiation with ultraviolet light induces chemical degradation of chlorpromazine. These phenomena are discussed in relation to chlorpromazine induced lupoid syndrome with antinuclear factors in the blood serum of human patients as well as to photo toxic and photo allergic dermatoses. 12 references. (Author abstract)

199961 Bevan, P.; Bradshaw, C. M.; Roberts, M. H. T.; Szabadi, E. Department of Psychiatry, University of Edinburgh, Morningside Park, Edinburgh, EH10 5HF, Scotland **The effect of microelectrophoretically applied mescaline on cortical neurones.** Neuropharmacology (Oxford). 13(10/11):1033-1045, 1974.

The effects of microelectrophoretically applied mescaline upon single cortical neurons were studied in the halothan anaesthetized cat. It was found that mescaline could exert both excitatory and depressant actions on cortical neurons. Comparison of the agonistic effects of mescaline with those of noradrenaline (NA) and 5-hydroxytryptamine (5-HT) revealed a high correlation between the effects of mescaline and NA. When a neuron responded in opposite directions to NA and 5-HT, the response to mescaline was invariably in the same direction as the response to NA. Mescaline appeared to be less

potent than NA and 5-HT. Responses to mescaline could be reversibly antagonized by the beta-adrenoceptor blocking agent, sotalol, and the 5-HT antagonist, methysergide. Both antagonists failed to discriminate between the agonistic effects of mescaline, NA and 5-HT, but antagonized responses to all three monoamines without affecting responses to acetylcholine. These results are interpreted in terms of an action of mescaline on monoamine receptors on cortical neurones. 19 references. (Author abstract modified)

199962 De Olveira, Luiz F.; Bretas, Alma D. Laboratorio de Neurofarmacologia, Instituto de Ciencias Biomedicas, U.F.R.J., Cidade Universitaria, Rio de Janeiro, 20.000, Brasil **Effects of 5-hydroxytryptophan, iproniazid and p-chlorophenylalanine on lidocaine seizure threshold of mice.** European Journal of Pharmacology (Amsterdam). 29(1):5-9, 1974.

The effects of 5-hydroxytryptophan (5-HTP), iproniazid and p-chlorophenylalanine (p-CPA) on the lidocaine seizure threshold of mice were studied. The median convulsant dose (CD50) of lidocaine in control (saline treated) mice was 76.0mg/kg. Pretreatment with 5-HTP (100mg/kg i.p.)lowered the CD50 to 61.0mg/kg. Similar results were observed in the iproniazid pretreated group. In the iproniazid 5-HTP treated group, a more pronounced and significant drop of the CD50 to 45.0mg/kg was observed. In p-CPA pretreated mice, the CD50 increased slightly to 90.0mg/kg. The duration of seizures increased in 5-HTP and iproniazid pretreated groups. These results suggest the possibility of an involvement of 5-HT in the lidocaine induced convulsive process. 23 references. (Author abstract)

199964 Cavero, Icilio; Lokhandwala, Mustafa F.; Buckley, Joseph P.; Jandhyala, Bhagavan S. L.E.R.S., Synthe Labo, 58 Rue de la Glaciere, 75621 Paris, Cedex 13, France **The effect of (-)-delta9-trans-tetrahydrocannabinol on myocardial contractility and venous return in anesthetized dogs.** European Journal of Pharmacology (Amsterdam). 29(1):74-82, 1974.

The effect of (-)-delta9-trans-tetrahydrocannabinol (THC) on myocardial contractility and venous return in anesthetized dogs was studied. Administration of THC to pentobarbital-anesthetized dogs in which heartrate was maintained constant by electrical pacing, decreased aortic blood pressure, cardiac output, left ventricular peak pressure and left ventricular end diastolic pressure and dP/dt. The contractility index was not altered by the compound. In dogs in which cardiac output was maintained constant by a right heart bypass procedure THC decreased blood pressure and total peripheral resistance and augmented intravascular blood volume. These observations support the hypothesis that the diminution of cardiac output induced by THC in animals with constant cardiac rate is primarily due to diminished venous return to the heart and not to an impaired ability of the myocardium. 19 references. (Author abstract modified)

199965 Wallach, Marshall B.; Hine, Bromfield; Gershon, Samuel. Department of Experimental Pharmacology, Syntex Research, 3401 Hillview Avenue, Palo Alto, CA 94304 **Cross tolerance or tachyphylaxis among various psychotomimetic agents on cats.** European Journal of Pharmacology (Amsterdam). 29(1):89-92, 1974.

Crosstolerance or tachyphylaxis among various psychotomimetic agents on cats were examined. DOM, 2,5-dimethoxy-4-methylamphetamine, a perception distorting psychotomimetic agent, has been demonstrated to elicit a marked behavioral syndrome in cats. This syndrome is antagonized by a pretreatment of DOM. This tachyphylaxis has been examined to determine the ability of various other types of psychotomimetic agents to antagonize the DOM induced syndrome. Mescaline and d-LSD but not l-LSD could prevent the occurrence of the DOM induced behavior. Ditran, tryptamine and d-amphetamine did not antagonize DOM. Thus it appears that the perception distorting psychotomimetic agents exhibit either cross tachyphylaxis or cross tolerance and may share a common mechanism of action. 11 references. (Author abstract)

199966 Collard, Keith J.; Roberts, Malcolm H. T. Department of Physiology, University College, P.O. Box 78, Cardiff CF1 XL, Wales **Effects of chlorimipramine on experimentally induced changes in forebrain 5-hydroxy-indoles.** European Journal of Pharmacology (Amsterdam). 29(1):154-160, 1974.

Changes in rat forebrain concentrations of 5-hydroxytryptamine(5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) were investigated following electrical stimulation of nucleus raphe medianus, or the administration of L-tryptophan. The effects of chlorimipramine upon the two treatments, were compared. Raphe stimulation elevated 5-HIAA and slightly reduced the 5-HT concentration. Pretreatment with chlorimipramine significantly reduced the stimulus induced elevation of 5-HIAA and proportionately increased the concentration of 5-HT. The administration of L-tryptophan produced significant increases in the forebrain concentration of both 5-HT and 5-HIAA. These findings provide additional support to the postulate that the elevation of 5-HIAA concentration following raphe stimulation arises from the extraneuronal release of 5-HT followed by uptake and catabolism. It is concluded that the effects of chlorimipramine upon brain 5-HT systems become evident when these systems are activated. 25 references. (Author abstract modified)

199967 Huang, Jen-Tzaw; Ho, Beng T. Department of Pharmacology, University of Minnesota, Minneapolis, MN 55455 **Effects of nikethamide, picrotoxin and strychnine on 'amphetamine-state'.** European Journal of Pharmacology (Amsterdam). 29(1):175-178, 1974.

The effects of nikethamide, picrotoxin and strychine on amphetamine-state were studied in the rat. Rats were trained to discriminate between d-amphetamine sulfate or saline by selectively pressing two levers programmed on differential response at low rate 15-sec schedule for food reinforcement. Nikethamide, strychnine and picrotoxin did not produce d-amphetamine-like responding in the animals. Results indicated that in order for drugs to produce similar discriminative cue they should possess a specific pharmacological property in common. 9 references. (Author abstract)

199999 Zigmond, R. E.; Mackay, A. V. P.; Iversen, L. L. MRC Neurochemical Pharmacology Unit, Medical School, Hills Road, Cambridge CB2 2QD, England **Minimum duration of trans-synaptic stimulation required for the induction of tyrosine hydroxylase by reserpine in the rat superior cervical ganglion.** Journal of Neurochemistry. 23(2):355-358, 1974.

The period during which transsynaptic stimulation is required by the rat superior cervical ganglion for induction of tyrosine hydroxylase by reserpine was studied. Ganglia were decentralized on one side at various times before or after an injection of reserpine. The tyrosine hydroxylase activity of the denervated and control ganglia was assayed 72 h after drug treatment. When decentralization was performed 8 h after an injection of reserpine, the increase in tyrosine hydroxylase activity was blocked in the denervated ganglia. Decentralization 12 h after reserpine treatment or later had no effect on the en-

zyme induction. The actual increase in tyrosine hydroxylase activity occurred between 24 and 48 h after injection of reserpine. 13 references. (Author abstract)

200002 Buchar, E.; Masek, K.; Janku, I.; Seifert, J.; Ostrovskaya, R. U. Institute of Pharmacology, Czechoslovak Academy of Sciences, Prague, Czechoslovakia **Effect of aminooxyacetic acid on the metabolism of pentobarbital in mice.** Journal of Neurochemistry (Oxford). 23(2):447-449, 1974.

The mechanism by which aminooxyacetic acid (AOAA) potentiates pentobarbital hypnosis was examined in mice. Onset of sleep was found to be much more rapid and the duration of sleep longer in animals treated with 30mg/kg AOAA. The results suggest that the administration of AOAA has a biphasic effect on pentobarbital tissue and plasma levels. Fifteen minutes after pentobarbital administration the level of labeled pentobarbital in blood, liver and brain was significantly lower in mice treated with AOAA; 45-60 min after injection the level of unmetabolized barbiturate was significantly higher. Since energy production is necessary for the maintenance of normal cell membrane functions as well as for the proper function of enzymes, it is suggested that the influence of AOAA is due to its interference with the energy forming cycle. 7 references.

200004 Fuller, Ray W.; Perry, Kenneth W.; Baker, John C.; Parli, C. John; Lee, Nancy; Day, William A.; Molloy, Bryan B. Lilly Research Laboratories, Eli Lilly & Co., Indianapolis, IN **Comparison of the oxime and the hydroxylamine derivatives of 4-chloroamphetamine as depletors of brain 5-hydroxyindoles.** Biochemical Pharmacology (Oxford). 23(23):3267-3272, 1974.

Brain 5-hydroxyindol levels were measured 6 hr after the injection of 4-chloroamphetamine and two of its possible metabolites--the oxime and the hydroxylamine. Both 4-chloroamphetamine and N-hydroxy-4-chloroamphetamine at 0.1mmole/kg caused marked reduction of serotonin and of 5-hydroxyindoleacetic acid levels, whereas the oxime had only a slight effect on serotonin levels. The N-hydroxy derivative appeared to be almost completely reduced to 4-chloroamphetamine in vivo, for it produced brain levels of 4-chloroamphetamine equivalent to those produced by 4-chloroamphetamine itself and lowered brain 5-hydroxyindole levels as much as did 4-chloroamphetamine at three different dose levels. The results make it seem unlikely that 4-chloroamphetamine's depletion of brain serotonin and 5-hydroxyindoleacetic acid is mediated by the conversion of 4-chloroamphetamine to these metabolites. 7 references. (Author abstract)

200021 Dubinskaya, G. R.; Nemtsov, A. V. Moscow Scientific-Experimental Institute of Psychiatry, Moscow, USSR **/The neuron ultrastructure in some brain areas during a long-term administration of aminazine and stelazine.**/ Ul0trastruktura neyronov kekotorikh otdelov golovnogo mozga pri dlitel0nom vvedenii aminazina i stelazina. Zhurnal Nevropatologii i Psikhiatrii Imeni S. S. Korsakov (Moskva). 74(8):1233-1239, 1974.

The effect of long-term administration of aminazine and stelazine on the ultrastructure of neurons in various portions of the brain was studied. The areas chosen were the sensorimotor and visual areas of the cortex, gigantic cell nuclei of the stem reticular formation, and the ventrolateral nuclei of the thalamus. Doses of 1mg/kg were given daily for 14 days to rats. Statistical analysis of the changes to the 191 neurons and 249 synapses involved showed that both neuroleptics caused a swelling of the mitochondria, enlargement of the endoplasmatic reticulum, hypertrophy of the Golgi apparatus, and a decreased amount of ribosomes in the polysomes. Aminazine caused greater changes in the mitochondria and an increase in the amount of synaptic vesicles in the terminals; stelazine led to a decrease in the latter. 16 references. (Journal abstract modified)

200033 Muller, Walter E.; Wollert, Uwe. Pharmakologisches Institut der Universitat, D-6500 Mainz, Obere Zahlbacher Strasse 67, Germany **Binding of d- and l-oxazepam hemisuccinate to bovine serum albumin.** Research Communications in Chemical Pathology and Pharmacology. 9(3):413-420, 1974.

D- and l-oxazepam hemisuccinate (RV 12o8 and RV121o) were found to bind to bovine serum albumin stereospecifically. The affinity constant (K1) of RV 12o8 is nearly threefold greater than that of RV 121o. RV 12o8 has three binding sites on the bovine serum albumin molecule whereas RV 121o only one. The unusual high difference in the binding of both enantiomers to human and bovine serum albumin is discussed regarding the affinities of the enantiomers to both albumins, the number of binding sites, and the degree of stereospecific binding. 10 references. (Author abstract)

200034 Waller, M. B.; Myers, R. D. Laboratory of Neuropsychology, Purdue University, Lafayette, IN 47907 **Similar actions of intra-hypothalamic 5,6-DHT and 5-HT in evoking hyperthermia in the monkey.** Research Communications in Chemical Pathology and Pharmacology. 9(3):421-429, 1974.

The effect of an injection of 5,6-dihydroxytryptamine (5,6-DHT) into the diencephalon of the monkey was studied. In the unanesthetized rhesus monkey, 5-HT or 5,6-DHT induces hyperthermia when either is microinjected directly into the anterior hypothalamus. The latency and magnitude of the 5,6-DHT fever is similar to that observed when 5-HT is applied to the same hypothalamic sites of the primate. When 5-HT is reinjected following a 5,6-DHT injection, a rise in temperature is elicited that is comparable to that seen earlier. Both 5-HT and 5,6-DHT evoked fevers are attenuated with equal efficacy by the antipyretic, acetaminophen. These results suggest a direct agonistic action of 5,6-DHT on postsynaptic 5-HT receptor sites and delayed response due to 5,6-DHT induced functional damage to serotonergic nerve terminals which causes a subsequent presynaptic release of 5-HT. 16 references. (Author abstract modified)

200035 Karler, Ralph; Cely, William; Turkanis, Stuart A. Department of Pharmacology, University of Utah College of Medicine, Salt Lake City, UT 84132 **Anticonvulsant activity of delta9-tetrahydrocannabinol and its 11-hydroxy and 8alpha,11-dihydroxy metabolites in the frog.** Research Communications and Chemical Pathology Pharmacology. 9(3):441-452, 1974.

The anticonvulsant activity of delta9-tetrahydrocannabinol (THC) and its metabolites was examined in the frog. In the frog (Rana pipiens) THC exhibited pronounced anticonvulsant activity against maximal electroshock. A study of the metabolic fate of THC demonstrated that THC is rapidly metabolized to several unidentified metabolites, as well as to mono and dihydroxylated products; brain amounts of both the hydroxylated metabolites and THC were measured as a function of time, but none of these measurements correlated quantitatively with the time course of anticonvulsant activity. Both 11-hydroxy- and 8alpha,11-dihydroxy-delta9-THC metabolites displayed anticonvulsant activity. All the cannabinoids tested were much more potent in the frog than in the rat or mouse; but there was no such disparity in the potency of diphenylhydantoin and phenobarbital in the different species. 15 references. (Author abstract modified)

200037 Nair, Xina. Miami Valley Laboratories, Proctor & Gamble Co., Cincinnati, OH 45239 **Contractile responses of guinea pig umbilical arteries to various hallucinogenic agents.** Research Communications in Chemical Pathology and Pharmacology. 9(3):535-542, 1974.

The contractile responses of helically cut guinea pig umbilical arteries to lysergic acid diethylamide (LSD), mescaline, psilocin and psilocybin were studied isometrically both in the presence and absence of 2-bromolysergic acid diethylamide (BOL-148) and cinanserin. Arteries were responsive to all four hallucinogens at low concentrations. 2-Bromolysergic acid diethylamide significantly antagonized the responses to mescaline, psilocin and psilocybin but only slightly to that of LSD. Cinanserin failed to inhibit the responses to either LSD or psilocin or psilocybin. 9 references. (Author abstract)

200041 Freidman, E.; Gershon, S. Department of Psychiatry, NYU Medical Center, 550 First Avenue, New York, NY 10016 **Effect of delta8-THC on alcohol-induced sleeping time in the rat.** Psychopharmacologia (Berlin). 39(3):193-198, 1974.

The effect of acute and repeated delta8-tetrahydrocannabinol (THC) administration on alcohol-induced sleeping time was studied in male albino rats. We have observed that acute pretreatment with THC markedly potentiates alcohol-induced sleeping time in a dose-related manner. This potentiation of the alcohol sleeping time is shortened significantly after repeated prior treatment with THC and can be observed 72 hrs postchronic treatment. The effect of THC on alcohol-induced sleeping time is not associated with an altered alcohol metabolism rate. 17 references. (Author abstract)

200044 Mulas, Angioletta; Mulas, Maria Luisa; Pepeu, Giancarlo. Department of Pharmacology, Florence University, Medical School, I-50133, Florence, Italy **Effect of limbic system lesions on acetylcholine release from the cerebral cortex of the rat.** Psychopharmacologia (Berlin). 39(3):223-230, 1974.

The effect of electrocoagulative lesions placed in the septum, fornix and fimbria, fimbria and hippocampus on acetylcholine (ACh) release from the cerebral cortex was investigated in rats under urethane anaesthesia. At least 2 weeks elapsed between the stereotactic placement of the lesions and the determination of ACh output. ACh was determined by bioassay on the dorsal muscle of the leech. No lesion affected the spontaneous release of ACh. The increase in ACh output induced by administration of amphetamine was abolished by the septal lesion only. On the other hand, the increase in ACh output induced by administration of scopolamine was strongly reduced by lesions of the septum, of the fornix and fimbria and to a lesser extent of the fimbria. The administration of amphetamine and scopolamine discloses therefore a specific functional impairment of the cerebral cholinergic mechanisms in rats with limbic lesions. 24 references. (Author abstract)

200045 Ferri, S.; Santagostino, A.; Braga, P. C.; Galatulas, I. Istituto di Farmacologia, Via Vanvitelli 32, I-20129 Milano, Italy **Decreased antinociceptive effect of morphine in rats treated intraventricularly with prostaglandin E1.** Psychopharmacologia (Berlin). 39(3):231-235, 1974.

Decreased antinociceptive effect of morphine in rats treated intraventricularly with prostaglandin E1 is reported. The administration of prostaglandin E1 intracerebrally through a cannula implanted in a lateral centricle, antagonizes morphine analgesia in rats. An electrical stimulation technique was adopted on the rat's tail to measure the antinociceptive activity of morphine. Some hypotheses are advanced in order to explain the sensitizing activity of prostaglandin E1. 17 references. (Author abstract)

200052 Stevens, J.; Wilson, K.; Foote, W. University of Oregon Medical School, 3181 S.W. Sam Jackson Park Road, Portland, OR 97201 **GABA blockade, dopamine and schizophrenia: experimental studies in the cat.** Psychopharmacologia (Berlin). 39(2):105-119, 1974.

The effects of blocking putative gamma-aminobutyric acid (GABA) inhibition on dopamine cells of origin in ventral tegmental area and substantia nigra were examined in freely moving cats with chronically implanted cannulas and recording electrodes. Instillation of the GABA blocking agent bicuculline in ventral tegmental area induces arousal, searching, slinking, hiding, evidence of fear, catatonic stance, staring and sniffing behaviors which were accompanied by spike activity from nucleus accumbens in several animals. Similar amounts of bicuculline placed in substantia nigra did not induce fear but were followed by ipsilateral grooming, circling and hyperesthesia, with EEG spiking in caudate nucleus and medial and lateral geniculate nuclei in several animals. The relationship of these findings to dopamine-induced stereotypies in mesolimbic and nigrostriatal systems and to evidence of dopamine excess or hypersensitivity in limbic striatum in patients with schizophrenic disorders is considered. 36 references. (Author abstract)

200053 Herz, A.; Blasig, J.; Papeschi, R. Department of Neuropharmacology, Max-Planck-Institut fur Psychiatrie, Munchen, Germany **Role of catecholaminergic mechanisms in the expression of the morphine abstinence syndrome in rats.** Psychopharmacologia (Berlin). 39(2):121-143, 1974.

The effect of various drugs affecting catecholaminergic (CA) mechanisms on the precipitated morphine withdrawal syndrome was studied in rats which had developed a medium degree of dependence. Administration of low doses of d-amphetamine, cocaine, and L-Dopa shortly before precipitating withdrawal by levallorphan induced a dose dependent increase of dominant withdrawal signs such as jumping and a decrease of recessive signs such as wet dog shaking; signs such as diarrhea and ptosis decreased, whereas rhinorrhea, salivation and lacrimation increased. The effects of the above drugs are interpreted as potentiation of withdrawal. Activation of noradrenergic or dopaminergic mechanisms with desipramine or apomorphine induced an increase in the intensity of withdrawal, which was, however, much more pronounced after the former than the latter drug. It is concluded that of both brain CA especially noradrenaline is involved in the manifestation of the morphine withdrawal syndrome. 45 references. (Author abstract modified)

200056 Rieger, H.; Krieglstein, J. Neuro-Psychiatric Klinik der Universitat Mainz, D-6500 Mainz, Langenbeckstrasse 1, Germany **Quantitative analysis of the EEG effects produced by imipramine, desipramine, promazine, and monodesmethyl promazine in the isolated perfused rat brain.** Psychopharmacologia (Berlin). 39(2):163-179, 1974.

The effects of imipramine, desipramine, promazine and monodesmethyl promazine on the electroencephalogram (EEG) of the isolated perfused rat brain were studied. The drugs produced clear EEG changes compared with the control EEG. An increase of the amplitude and a slowing of the frequency were found for all drugs. Only the changes produced by desipramine were not statistically significant. Furthermore, imipramine and promazine provoked grouped spikes, whereas monodesmethyl promazine caused grouped

sharp waves; such characteristic patterns could not be observed after desipramine. The pronounced similarity of the EEG effects produced by imipramine and promazine as well as the clear difference between the imipramine and desipramine effects were pointed out as the most striking results. It was suggested that imipramine becomes a typical antidepressant in the whole organism after demethylation. 38 references. (Author abstract modified)

200058 Greengrass, Pamela M.; Tonge, Sally R. Research Department, Ciba-Geigy Ltd., CH-4002 Basel, Switzerland **The accumulation of noradrenaline and 5-hydroxytryptamine in three regions of mouse brain after tetrabenazine and iproniazid: effects of ethinyloestradiol and progesterone.** Psychopharmacologia (Berlin). 39(2):187-191, 1974.

The effects of the hormones on monoamine synthesis was studied in mice. Four groups of ovariectomized mice were injected with tetrabenazine, 12 hrs later, one group was injected with iproniazid, one with iproniazid and ethinyloestradiol, and one with iproniazid and progesterone. All mice were killed 4 hrs after the iproniazid injection (16 hrs after tetrabenazine) and noradrenaline and 5-hydroxytryptamine concentrations were determined in three regions of the brains: the forebrain (cortex, hippocampus), the middle brain (hypothalamus, thalamus, striatum), and the hindbrain (midbrain, pons, medulla, cerebellum). Ethinyloestradiol increased the accumulation of noradrenaline in the fore and middlebrain regions; progesterone decreased the accumulation of noradrenaline in the fore and middle brain regions and of 5-hydroxytryptamine in the middle and hindbrain regions. 14 references. (Author abstract modified)

200064 Sabelli, H. C.; Bartizal, F.; Giardina, W. J.; Myles, S. B. Department of Pharmacology, Chicago Medical School, 2020 West Ogden Avenue, Chicago, IL 60612 **Effects of alpha-adrenergic blockers on visual evoked responses in rabbits.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 33(3):321-324, 1972.

The effects induced by systematic administration of alpha-adrenergic blockers of the alpha-adrenergic receptors on the visual evoked response were examined. In nonanesthetized rabbits, the blockers of alpha-adrenergic receptors markedly modified the cortical potentials evoked by optic stimuli and also partially prevent the effect of L-Dopa. 10 references. (Author abstract)

200078 Albus, K.; Herz, A. Max-Planck-Institut fur Biophysikalische Chemie, Abtlg. Neurobiologie, 34 Gottingen-Nikolausberg, Germany **Inhibition of behavioural and EEG activation induced by morphine acting on lower brain-stem structures.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 33(6):579-590, 1972.

The changes of spontaneous electroencephalogram (EEG) and behavior and of EEG activation induced by nociceptive (tooth pulp or hind paw) and nonnociceptive (acoustic, tactile) stimuli and by electrical stimulation of the reticular formation (RF) were investigated in rabbits with chronically implanted electrodes for the application of morphine. There was no clear correlation between the inhibition of EEG response to nociceptive reaction. Both reactions were found to be inhibited at times when the EEG activation induced by stimulation of the RF was unchanged. When morphine was allowed to spread in the anterior parts of the VS (lateral ventricles, 3rd ventricle) only minor changes were observed. It is concluded that the deactivating effects on behavior and the EEG are mediated by structures bordering the VS, especially those in the vicinity of the 4th ventricle. Experiments in which the spread of intraventricular morphine was checked autoradiographically indicate that only peripheral regions of the RF of the brainstem are reached by the drug when these effects are manifest. It is suggested that morphine probably does not cause sedation and EEG deactivation by a direct action on the RF but rather by indirect mechanisms. 35 references. (Author abstract modified)

200081 Fernstrom, John D.; Shabshelowitz, Harlan; Faller, Douglas V. Department of Nutrition and Food Science, MIT, Cambridge, MA 02139 **Diazepam increases 5-hydroxyindole concentrations in rat brain and spinal cord.** Life Sciences (Oxford). 15(9):1577-1584, 1974.

Diazepam elevates serotonin (5HT) and 5-hydroxyindoleacetic acid (5HIAA) concentrations in rat brain and spinal cord. The maximal effect occurs 1-2 hrs after drug injection and is dose related between 5-20mg/kg (intraperitoneal). The action of diazepam on brain 5HT and 5HIAA 1 hour before drug injection enhances the diazepam induced increase in brain indoles; consumption of a diet that lowers brain 5HT and 5HIAA partially blocks the elevation in brain indoles that follows diazepam injection. 12 references. (Author abstract)

200082 Marquardt, Gerald M.; DiStefano, Victor. Department of Pharmacology and Toxicology, University of Rochester School of Medicine and Dentistry, Rochester, NY 14642 **The hepatic microsomal metabolism of beta-3,4-methylenedioxyamphetamine (MDA).** Life Sciences (Oxford). 15(9):1603-1610, 1974.

The conversion of beta-3,4-methylenedioxyamphetamine (MDA) to alpha-MeDA by rat liver microsomes in vitro was examined. Rat liver microsomes were shown to catalyze the conversion of MDA to a metabolite identified as alpha-MeDA. Characterization of this enzyme system strongly suggests that this conversion is catalyzed by the microsomal NADPH-dependent cytochrome P-450 hydroxylase known to catalyze the demethylenation of other methylenedioxyphenyl compounds. The relative constancy of the sum of MDA and alpha-MeDA, observed throughout all incubations, suggests that MDA is metabolized to only alpha-MeDA and that alpha-MeDA is not further metabolized under these conditions. A kinetic analysis of microsomal metabolism of MDA to alpha-MeDA suggests the involvement of only one homogeneous enzyme system. 18 references. (Author abstract)

200088 Westheimer, Ruth; Klawans, Harold L. Rush Medical College, Chicago, IL **The role of serotonin in the pathophysiology of myoclonic seizures associated with acute imipramine toxicity.** Neurology. 24(12):1175-1177, 1974.

Since myoclonic seizures can be generated in guinea-pigs with 5-hydroxytryptophan, the precursor of serotonin, and since imipramine has been observed to decrease the reuptake to serotonin in the brain, an attempt was made to potentiate 5-hydroxytryptophan-induced myoclonus in guinea-pigs with imipramine. Subthreshold doses of 5-hydroxytryptophan together with 35mg/kg of imipramine consistently led to myoclonic seizures in the animals. Antagonists of norepinephrine, dopamine, and acetylcholine all failed to block the potentiation of 5-hydroxytryptophan-induced seizures with imipramine. These results are consistent with the hypothesis that imipramine acts via serotonergic mechanisms in the brain to produce myoclonic seizures. 15 references. (Author abstract modified)

200313 Chiueh, Chuang Chin. Michigan State University **The in vivo release of endogenously synthesized catecholamines from**

the cat brain by lateral hypothalamic stimulation and by d-amphetamine administration. (Ph.D. dissertation). Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-19795 HC$12.50 MF$4.00 167 p.

The in vivo release of endogenously synthesized dopamine from the nigrostriatal neurons in response to appropriate stimuli was demonstrated. A cerebroventricular perfusion technique was utilized to detect the efflux of endogenously synthesized dopamine and/or norepinephrine from the cat brain into a ventricular perfusate. Radioactive tyrosine or DOPA, administered i.v.,was converted to catecholamines in brain tissues lining the cerebroventricular system. Most of the lateral hypothalamic stimulation induced efflux of 3H-dopamine and virtually all the efflux of 3H-norepinephrine originated from structures lining the anterior horn of the lateral ventricle. It was concluded that newly-synthesized striatal dopamine plays a more important role in the maintenance of amine release by d-amphetamine than does mobilization of stored dopamine. (Journal abstract modified)

200565 Arushanyan, E. B.; Stolyarov, G. V.; Tolpyshev, B. A. Chita Medical Institute, Chita, USSR /**The influence of alpha-methyltyrosine and disulfiram on the inhibitory function of the caudate nucleus and catecholamine content in the brain of cats.**/ Vliyaniye a-metiltirozina i disul0firama na tormoznuyu funktsiyu khvostatogo yadra i soderzhaniye katekholaminov v mozge koshek. Byulleten0 eksperimental0noy biologii i meditsiny (Moskva). 77(2):48-51, 1974.

The effect of alpha-methyltyrosine and disulfiram on the inhibitory function of the brain was studied in cats with unrestricted movement by measuring changes in the inhibitory function of the caudate nucleus and catecholamine content. Alpha-methyltyrosine was found to diminish the threshold of behavior arrest reaction caused by low frequency stimulation of the head of the caudate nucleus. This coincided with a reduction of the catecholamine level in the neostriatum and the brainstem. Since a selective reduction of the concentration of stem noradrenaline under the influence of disulfiram was not accompanied by any intensification of movement arrest, the reaction was concluded to depend upon the nigrostriatal dopaminergic mechanisms. Both alpha-methyltyrosine and disulfiram were found to facilitate the appearance of caudate spindles on the electrocorticogram in stimulation of the caudate nucleus. 15 references. (Journal abstract modified)

200566 Komissarov, I. V.; Talalayenko, A. N. Donezk Medical Institute, Donezk, USSR /**The influence of catecholamines, serotonin, and some amino acids administered into the amygdaloid complex on conditioned reflexes of avoidance and motor activity in rats.**/ O vliyanii katekholaminov, serotonina i nekotorykh aminokislot, vvodimykh v mindalevidnyy kompleks na uslovnuyu reaktsiyu izbeganiya i dvigatel0nuyu aktivnost0krys. Byulleten0 eksperimental0noy biologii i meditsiny (Moskva). 77(2):51-55, 1974.

Effects of catecholamines, serotonin and amino acids injected into dorsomedial portions of the amgdala on the latent time of conditioned reflex motor activity and muscular tone were studied in rats. Dopamine, serotonin and asparaginic acid significantly increased the latent time of the avoidance reflex, and stimulated motor activity. Dopamine effects were depressed by haloperidol, but not by phentholamine, chlorpromazine or deseryl. Serotonin effects were prevented by dihydroergotamine, deseryl, and chlorpromazine, but not by phenolamine, morphine or haloperidol. Bioamine antagonists were inactive against revealed effects of asparaginic acid. Reflex latent time was reduced by noradrenaline and increased by GABA in doses which failed to alter muscle tone or motor activity. Noradrenaline effects were eliminated by phentholamine, chlorpromazine, and dihydroergotamine, but not by propranolol. Monoamine antagonists failed to inhibit conditioned avoidance reflexes caused by GABA. Results confirm participation of alpha-adrenergic, serotonergic, or dopaminergic structures of amygdaloid complex neurons in the observed effect of monoamines. 20 references. (Journal abstract modified)

200751 Abreu, Luiz A.; Abreu, R. Raposo. Laboratory of Biochemistry, Instituto Oswaldo Cruz, P. O. Box 926-ZC-00, Rio de Janeiro, Brazil **Effect of long-term lithium treatment on brain fumarase activity.** Experientia (Basel). 30(9):1056-1057, 1974.

The effect of long-term lithium treatment on brain fumarase activity was investigated in mice. Treatment with lithium carbonate did not influence the weights of the animals. A significant increase of the specific fumarase activity was observed in Li+-treated mice. Results of experiments to demonstrate an in vitro effect of Li+ were negative. Addition of lithium carbonate up to 10mg/ml of the homogenate and incubation for 15 minutes before fumarase determination did not change the enzyme activity. The data suggest that the effects of lithium on three enzymes of the Krebs cycle (fumarase, succinate dehydrogenase, and aconitase) are indirect. The lack of knowledge of Li+ mechanism of action precludes an exact evaluation of the role of these enzymes in manic-depressive psychosis. 9 references.

200752 Stanisstreet, M. Department of Zoology, University of Liverpool, P. O. Box 147, Liverpool L69 38X, England **Comparison of the effects of lithium, beta-phenylethylamine and tyrosine on Xenopus embryos.** Experentia (Basel). 30(9):1081-1082, 1974.

The effects of lithium chloride, beta-phenylethylamine and tyrosine on amphibian (Xenopus) embryos are described. A range of abnormalities were found in the experiments: exogastrulae without neural structures; embryos in which the neural folds were separated by protruding yolky cells; and neurulae in which the ventral region was expanded. It is suggested that these deformities are the result of an excessive production of endoderm cells or vegetalization of the embryos. Other abnormalities occurred less frequently and were usually defects in the neural structures. Tyrosine did not produce vegetalization in embryos at stages when lithium did so, but exposure to beta-phenylethylamine produced a range of abnormalities similar to that produced by lithium. These results suggest that lithium and beta-phenylethylamine produce a similar effect, vegetalization, in the amphibian embryo. The embryo appears more susceptible during early cleavage and is less susceptible by the late blastula stage. 10 references.

201005 Speciale, Samuel Gene, Jr. Loyola University of Chicago **The relationship of central monoamines to drug-induced sleep in the rat, examined on a 24-hour basis. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-16970 HC$12.50 MF$4.00 398 p.

The influence of CNS amines on pentobarbital (PB) and gamma-butyrolactone (GBL) sleep was examined in adult male rats and mice, adapted for at least 3 weeks to a programmed light-dark cycle. Sleep duration was determined at 0600, 1200, 1800 and 2400 hours after IP doses of PB (50mg/kg) or GBL (350mg/kg) in pretreated and control subjects. Data indicate that PB sleep is influenced by drugs affecting amine levels, body temperature and protein binding. It is augmented by rais-

ing brain levels of dopamine or by reducing serotonin levels, or by combinations of these effects. The probability that other amines must participate in these effects was inferred. Dopapargyline and pCPA altered amine levels, while direct depressant effects were seen with melatonin, histidine, and diphenhydramine. The significant reduction of amine levels by decaborane (DB) and its hypothermic effect combined to prolong PB sleep. Diphenhydramine also produced hypothermia. GBL sleep followed a 24 hr pattern resembling PB, although its mechanism remains unclear. The circadian patterns of GBL and PB sleep were similar. (Journal abstract modified)

201323 Yamaguchi, Kiyoko; Iwahara, Shinkuro. Department of Medical Psychology, Tokyo Metropolitan Institute for Neurosciences, Tokyo, Japan **Effects of chlordiazepoxide upon differential heart rate conditioning in rats.** Psychopharmacologia (Berlin). 39(1):71-79, 1974.

Chlordiazepoxide (CDP) at 20mg/kg, i.p. almost completely blocked classical differential conditioning in heartrate (HR) in unanesthetized rats. However, it only slightly, if at all, depressed simple HR conditioning to the same conditioned stimulus (CS). The simultaneously observed differential conditioning in respiratory rate (RR) was also inhibited by CDP with its little effect upon simple RR conditioning. Motor activity as measured by changes in electromyogram records immediately preceding and during the CS was not affected either by CDP or by the differential conditioning procedure. Results are explained in terms of the drug's disinhibitory action. 8 references. (Author abstract)

201324 Jacobs, Barry L. Department of Psychology, Princeton University, Princeton, NJ 08540 **Evidence for the functional interaction of two central neurotransmitters.** Psychopharmacologia (Berlin). 39(1):81-86, 1974.

Rats pretreated with pargyline and then given either L-tryptophan or L-dopa display strikingly similar behavioral syndromes, and therefore, it was hypothesized that they might be dependent upon a common neurochemical substrate. This hypothesis was tested by observing whether blocking either the biosynthesis of serotonin or dopamine or their receptors was capable of blocking the production of the syndrome produced by precursors of the other transmitter. Pretreatment with alpha-methyl-p-tyrosine, a catecholamine synthesis inhibitor, failed to affect either syndrome, whereas p-chlorophenylalanine, a serotonin synthesis inhibitor, blocked both. Similarly the dopamine receptor blocker pimozide had no effect on either syndrome, while the serotonin receptor blockers cinanserin and methysergide blocked or diminished both syndromes equally. It is concluded that at least a portion of the syndrome that emerges following pargyline and L-dopa is mediated by serotonin rather than dopamine. 12 references. (Author abstract modified)

201409 Bigler, Erin D.; Fleming, Donovan E.; Shearer, Donald E. Brigham Young University, Provo, UT 84602 **Pharmacological modulation of photically evoked afterdischarge patterns in hooded Long-Evans rats.** Bulletin of the Psychonomic Society. 4(3):179-181, 1974.

The pharmacological modulation of photically evoked afterdischarge (AD) patterns within a short-term habituation paradigm were examined in the hooded Long-Evans rat. Pharmacological arousal by amphetamine, pilocarpine, and physostigmine or induced thalamic suppression by trimethadione (Tridione) attenuated AD development. AD development was unaffected by saline, methyl atropine, and atropine. Pentylenetetrazol (Metrazol) was used as an AD potentiator and, as such, enhanced AD development following all drug conditions except within the physostigmine and methyl atropine sessions. It was determined that in the hooded rat AD varies only as a function of drug injected; time (habituation) was not a factor. The role of the reticulocortical projection system and the limbic system was incorporated in the explanation of the results. Significant differences were also noted between the pharmacology of AD parameters in hooded versus albino rats. 13 references. (Author abstract)

201479 Gusselnikov, V. I.; Iznak, A. F.; Mukhametov, L. M. Faculty of Biology, Moscow Univ., Moscow, 117234, USSR **Neuronal activity of nucleus caudates and thalamus during barbiturate spindles in rats.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 35(5):523-531, 1973.

The neuronal activity of the caudate nucleus (CN) and the thalamus during spontaneous barbiturate spindles and evoked caudate spindles was studied using extracellular and intracellular recording in curarized and lightly barbiturized rats. Changes in the impulse activity of the cells concomitant with the spindles were found in a majority of extracellularly recorded neurons of both the CN and thalamus. The spike discharges were locked to certain spindle wave phases. In the CN the neurons discharged mainly at the top of the positive peak of the spindle wave and in the thalamus at the negative wave preceding the positive peak. Rhythmic oscillations of the membrane potential during the spindles were recorded in 36 of 69 CN neurons and in 57 of 61 thalamic neurons. Rhythmic excitatory postsynaptic potentials (EPSPs) accompanied by spike discharges prevailed in the CN. Hyperpolarization was observed in a few neurons. In the thalamus, rhythmic inhibitory postsynaptic potentials were a constant component of cell activity during spindles. Differences between the neuronal activity of the CN and the thalamus appear to be due to the pacemaker role of the thalamus in the generation of spindles as opposed to that of the CN. 39 references. (Author abstract modified)

201888 Saramikov, A. S.; Spiridonova, Z. I.; Alekseeva, L. P. Tomsk Medical Institute, Tomsk, USSR /**Effect of lithium on the EEG and serotonin content in the brain.**/ Vliyaniye litiya na EEG i soderzhaniye serotonina v mosge. Byulleten0 Eksperimental0noy Biologii i Meditsiny (Moskva). 78(8):61-64, 1974.

The effect of lithium on serotonin content and EEG of the brain of rats and rabbits was studied. Lithium was injected in single doses of 200 and 450mg/kg for rats, 300mg/kg for rabbits. In the rats, serotonin content was reduced in the brainstem; in rabbits, it was reduced in the hypothalamus, reticular formation, and amygdala. The drug produced decreasing influence on the bioelectrical activity of the hypocampus and caudate nucleus of the amygdala which did not correlate with the changes in their serotonin content. 17 references. (Journal abstract modified)

201913 Zakusov, V. V. Institut farmakologii AMN SSSR, Moscow /**The influence of prolonged application of tranquilizers and antidepressants on the summational capacity of the central nervous system.**/ Vliyaniye trankvilizatorov i antidepressantov na summatsionnuyu sposobnost0 tsentral0noy nervnoy sistemy pri prodolzhitel0nom primenenii. Farmakologiya i Toksikologiya (Moskva). 37(4):389-391, 1974.

The influence of prolonged application of tranquilizers and antidepressants on the summational capacity of the central nervous system was studied in rabbits. Diazepam, phthoracizine, and imipramine were used. Repeated application over 30 days had the same effect on the summation of im-

pulses in the central nervous system as one time application: stimulation from small doses, depression from high doses. Diazepam and phthoracizine affected the stimulating capacity of the central nervous system more permanently as the result of prolonged application than did imipramine. 3 references. (Journal abstract modified)

201917 Titov, N. S.; Salyaev, V. N. Kafedra farmakologii, Yaroslav, USSR **/Influence of hexobarbital on the biosynthesis of catecholamines and their precursors in the brain.**/ O vliyanii geksenala na biosintez katekholaminov i ikh predshestvennikov v golovnom mozge. Farmakologiya i Toksikologiya (Moskva). 37(4):398-401, 1974.

The influence of hexobarbital on the biosynthesis of catecholamines was studied in rats. The distribution of monoamines and amino acid precursors over different parts of the brain was established. Hexobarbital was injected to induce anesthesia in doses of 70mg/kg. A nonuniform distribution of metabolites and a marked accumulation of dopamine over all parts of the brain resulted. As anesthesia developed, the norepinephrine content rose in the thalamus and cerebellum but did not change materially in the other portions. The hexobarbital induced anesthesia was attended by a slowed down metabolism of the amino acids phenylalanine and tyrosine. 10 references. (Journal abstract modified)

201920 Gilyadova, L. A. Tsentral0nyy nauchno-issledovatel0skiy institut sudebnoy psikhiatrii, Moscow **/Experimental study into immunological factors of resistance to chlorpromazine.**/ Eksperimental0noye izucheniye immunologicheskikh faktorov rezistentnosti k aminazinu. Farmakologiya i Toksikologiya (Moskva). 37(4):421-424, 1974.

The immunological factors of resistance to chlorpromazine were studied in rabbits, guinea-pigs, and mice. Animals which had received chlorpromazine for 2 weeks formed antibodies. Introduction of chlorpromazine together with serum containing these antibodies to chlorpromazine in mice resulted in a reduced muscle relaxant and cataleptic action of this neuroleptic. 22 references. (Journal abstract modified)

202165 Yanagida, Hisashi; Yamamura, Hideo. Dept. of Anesthesiology, Faculty of Medicine, University of Tokyo, Japan **Electroencephalographic study of the local transport of central nervous stimulants into the brain.** Advances in Neurological Sciences (Tokyo). 15(4):184-187, 1971.

The effect of central nervous stimulants on the EEG was studied in 12 cats treated with xanthinol nicotinate (1.5mg), CDP-choline (0.5mg), or caffeine and sodium benzoate (0.2mg) at the mesencephalic reticular formation, posterior hypothalamus and pontine reticular formation. The results show that xanthinol nicotinate injected into either one of the three areas deactivated the neocortical and hippocampal patterns; CDP-choline injected into the mesencephalic reticular formation and posterior hypothalamus induced neocortical and hippocampal seizure patterns; caffeine and sodium benzoate administered into either one of the three areas induced neocortical and hippocampal seizure patterns. 7 references. (Author abstract modified)

202191 Azzaro, Albert J.; Ziance, Ronald J.; Rutledge, Charles O. Department of Neurology, West Virginia University Medical Center, Morgantown, WV 26505 **The importance of neuronal uptake of amines for amphetamine-induced release of 3H-norepinephrine from isolated brain tissue.** Journal of Pharmacology and Experimental Therapeutics. 189(1):110-118, 1974.

The importance of neuronal uptake of amines for amphetamine-induced release of H-norepinephrine from isolated brain tissue is reported. Amphetamine inhibited the neuronal uptake and accumulation of 3H-norepinephrine into chopped rat brain tissue. Cocaine and desipramine were approximately equipotent with amphetamine in inhibiting neuronal uptake but differed in their ability to release the 3H-amine. Desipramine inhibited neuronal uptake maximally at concentrations which caused little or no release of 3H-norepinephrine. It is concluded that amphetamine-induced release of 3H-norepinephrine is not simply due to inhibition of neuronal uptake of spontaneously-released 3H-amine. The uptake of low concentrations of 3H-amphetamine into synaptosomes from cerebral cortex was markedly inhibited by cocaine and desipramine. These results indicate that amphetamine is transported by the neuronal uptake system and that cocaine and desipramine inhibit the release of 3H-norepinephrine at low concentrations of amphetamine by inhibiting the transport of amphetamine into the neuron. 31 references. (Author abstract modified)

202203 Anisman, Hymie; Kokkinidis, Larry. Department of Psychology, University of Waterloo, Waterloo, N2L 3G1, Ontario, Canada **Effects of central and peripheral adrenergic and cholinergic modification on time-dependent processes in avoidance performance.** Behavioral Biology. 10(2):161-171, 1974.

The effects of central and peripheral adrenergic and cholinergic modification on time dependent processes in avoidance performance were studied in rats. Following exposure to signaled inescapable shock, rats were tested in a shuttle avoidance task at one of three retention intervals (0.16, 1, or 0.24 hr). Administration of scopolamine or D-amphetamine was found to eliminate the U-shaped performance function ordinarily observed over these various retention intervals. Methyl scopolamine and hydroxyamphetamine did not affect the time dependent changes in avoidance performance. Septal lesions were found to eliminate the U-shaped function as was the case with scopolamine and D-amphetamine. Results were taken to indicate the involvement of central adrenergic and cholinergic mechanisms in producing time dependent changes in avoidance behavior. 37 references. (Author abstract)

202266 DeWyngaert, Mark; Kellogg, Carol. Univ. of Rochester, Rochester, NY **Effect of early L-dopa administration on the ontogeny of motor functions in the rat.** Research Report, NIMH Grant MH-23427, 1974, 11 p.

The effect of L-dopa administered in a subthreshold dose for motor hyperactivity in young rats during the first week of life is analyzed. Results of related research are cited. One hundred and two neonatal Long-Evans hooded rats were studied. Noticeable differences were observed at 10 and 14 days of age following the injection of the test dose (100mg/kg) of L-dopa; at 21 and 28 days, motor deficits were not observed in pretreated animals after the L-dopa test dose. It is concluded that interference with catecholamine transmission by small doses of L-dopa during the first 5 days of postnatal life in the rat induces motor impairment at certain stages of development, most evident when animals are stimulated to hyperactivity stages. The injection of small doses of L-dopa appears to be useful for elucidating development of related transmitter systems in the brain. 12 references.

202281 Duvoisin, R. C.; Marsden, C. D. Dept. of Neurology, Mount Sinai School of Medicine, Fifth Ave. at 100th St., New York, NY 10029 **Reversal of reserpine-induced bradykinesia by**

alpha-methyldopa -- new light on its modus operandi. Brain Research (Amsterdam). 71(1):178-182, 1974.

Reversal of reserpine-induced bradykinesia by alpha-methyldopa (AMD) was investigated. All features of the reserpine syndrome observed were reversed by AMD given 4 hours after reserpine by i.p. injection in mice in doses ranging from 100 to 1000mg/kg. The reversal was also found to be significantly antagonized by the centrally active decarboxylase inhibitors RO 4-4602 and NSD-1034, but not by methyldopahydrazine (MK-486). It was also antagonized by disulfuram and FLA 63. Chlorpromazine and phenoxybenzamine antagonized the AMD reversal, but pimozide did not. When administration of AMD was delayed until 24 hours after reserpinization, its effect was greatly reduced. This failure to reverse the reserpine syndrome suggests that intact amine storage granules are required for the reversal. 14 references.

202370 Bunney, B. S.; Aghajanian, G. K.; Roth, R. H. Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06519 **Amphetamine, L-dopa and apomorphine: effects on activity of rat dopaminergic neurons.** Federation Proceedings. 32(3):247, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effect of apomorphine (APO), amphetamine (AMP), and L-Dopa on the firing rate of dopamine (DA) containing cells in the substantia nigra and ventral tegmental area of the rat midbrain in the presence or absence of DA synthesis inhibitors was reported. Anesthetized and gallamine-paralyzed rats were used. All three drugs markedly depressed DA cell activity. Alpha-methyl-p-tyrosine (AMPT), which inhibits DA synthesis at the initial step, prevented or reversed the AMP-induced depression. L-Dopa, the immediate precursor of DA, overcame this antagonism. The L-Dopa inhibition of cell firing rate could be prevented by a central decarboxylase inhibitor which blocked the conversion of L-Dopa to DA. This latter antagonism could be overcome by APO. Thus the depression of dopaminergic cell activity by L-Dopa and AMP, but not APO, appears dependent on ongoing DA synthesis. (Author abstract modified)

202417 Smith, Howard E.; Burrows, Elizabeth P.; Miano, Jeffrey D.; Mount, Charles D.; Sanders-Bush, Elaine; Sulser, Fridolin. Dept. of Chemistry, Vanderbilt Univ., Nashville, TN 37235 **Action of (S)- and (R)-para-substituted amphetamine hydrochlorides and (alpha S)- and (alpha R)-p-chloronorephedrine and (alpha S)- and (alpha R)-p-chloronorpseudoephedrine hydrochlorides on the level of 5-hydroxytryptamine and the activity of tryptophan hydroxylase in rat brain.** Journal of Medicinal Chemistry. 17(4):416-421, 1974.

The action of substituted amphetamine hydrochlorides and chloronorephedrines and chloronorpseudoephedrine hydrochlorides on the level of 5-hydroxytryptamine (serotonin, 5-HT) and the activity of tryptophan hydroxylase (TH) was investigated in the rat brain. Both isomers of p-chloroamphetamine hydrochloride caused a reduction in the level of 5-HT and the activity of TH in the rat brain. The R isomer induced a more rapid decline in 5-HT which was of shorter duration. The effect of this isomer on TH activity disappeared 2 weeks after injection but the effects of the S isomer persisted. The results indicate that different mechanisms are involved in the short- and long-term effects. Both isomers of p-nitroamphetamine hydrochloride reduced 5-HT levels and TH activity 4 hours after injection with some recovery after 2 weeks. Since the isomers of p-chloronorephedrine hydrochloride and p-chloronorpseudoephedrine hydrochloride did not have a significant effect on the level of 5-HT or the activity of TH, beta-hydroxylation was not an important factor in either the short or long-term effects of p-chloroamphetamine hydrochloride in serotonergic neurons. 30 references. (Author abstract modified).

202422 Kameyama, Yoshiro; Hoshino, Kiyoshi; Miyamoto, Masaki; Hayasaka, Ikuo. Nagoya University, Japan **Developmental disturbance of the brain in rat offspring following maternal administration of 5-fluouracil during pregnancy.** Annual Report of the Research Institute of Environmental Medicine (Nagoya). 20:91-96, 1973.

The effect of 5-fluouracil (5-FU) on fetal brain development in pregnant Wistar rats receiving 40 to 60mg/kg of 5-FU on day 16 or 18 of pregnancy with fetal removal 24 to 48 hours postadministration was studied. In 40mg groups, damage was limited to the ventricular matrix and the migrating cell zone. In 60mg groups, damage included the primordial cortex. Under heavier dose, day of fetal removal affected extent of damage. Doses of 20mg administered under similar conditions did affect development of the dorsal neocortex. 9 references. (Author abstract modified)

202464 Bennett, James L.; Aghajanian, George K. Connecticut Mental Health Center, 34 Park St., New Haven, CT 06508 **D-LSD binding to brain homogenates: possible relationship to serotonin receptors.** Life Sciences (Oxford). 15(11):1935-1944, 1974.

The d-lysergic acid diethylamide (d-LSD) binding to brain homogenates was explored. Using a rapid filtration technique, stereospecific high affinity d-LSD binding was found in brain fractions from a number of subcortical and cortical rat brain areas. Among the putative neurotransmitters tested only serotonin effectively displaced d-LSD from this specific binding site. Only the serotonin displaceable component of binding is saturable in a high affinity range. No change was observed in specific d-LSD binding in forebrain homogenates from rats in which ascending serotonergic pathways were destroyed by lesions of the raphe nucleus. It is concluded that the majority of the d-LSD binding sites may be associated with a postsynaptic serotonin receptor rather than a presynaptic receptor associated with serotonergic inputs. 25 references. (Author abstract modified)

202599 Elaev, N. R. no address /**Incorporation of acetate (C14)(P;32) and phosphate into the brain lipids during blockage of the cholino- and adrenoreceptors.**/ Vklyucheniye atsetata i fosfata v lipidy mozga pri blokade kholino- i adrenoretseptorov. Byulleten0 eksperimental0noy biologii i meditsiny (Moskva). 78(9):60-61, 1974.

The effect of cholinolytic amyzil and adrenolytic haloperidol on incorporation of acetate and phosphate into brain lipids was investigated in rats. Amyzil and haloperidol were introduced intravenously into female rats weighing 200 to 250 grams. Radioactivity of the lipids was measured, and amyzil blockage of M-cholinoreceptors was found to be accompanied by depression of acetate and phosphate incorporation into the brain lipids; haloperidol blockage of alpha-adrenoreceptors activated these processes. Conduction of a nerve impulse into the cholinergic and adrenergic synapses of the brain was concluded to be accompanied by a change in lipid synthesis intensity. 13 references. (Journal abstract modified)

202662 Shoeman, Don W.; Sirtori, Cesare R.; Azarnoff, Daniel L. Clinical Pharmacology - Toxicology Center, 3800 Cambridge, KS 66015 **Inhibition of amphetamine tolerance and metabolism by propranolol.** Journal of Pharmacology and Experimental Therapeutics. 191(1):68-71, 1974.

Inhibition of amphetamine tolerance and metabolism by propranolol was studied. Rats received water or water containing 110mg of d-amphetamine per liter and ground lab chow or lab chow containing 1g of propranolol per kg of chow ad libitum for 30 days. Animals receiving no drug and propranolol fed animals gained weight; those receiving d-amphetamine alone lost weight during the first 14 days then gained weight, whereas those receiving both propranolol and d-amphetamine lost weight during the entire 30 days. Steady state plasma levels of d-amphetamine and the apparent volume of distribution of an intravenous tracer dose of 3H-amphetamine were determined. Steady state d-amphetamine levels were higher in animals receiving d-amphetamine and propranolol than in animals receiving only d-amphetamine. This increase in plasma level is due both to a decrease in elimination of d-amphetamine and a decrease in its volume of distribution. Propranolol blocks tolerance to the weight loss produced by d-amphetamine at least in part by increasing the plasma level of d-amphetamine achieved during treatment. 13 references. (Author abstract)

202664 Walters, Judith R.; Roth, Robert H. Department of Pharmacology, Yale University School of Medicine, 333 Cedar St., New Haven, CT 06510 **Dopaminergic neurons: drug-induced antagonism of the increase in tyrosine hydroxylase activity produced by cessation of impulse flow.** Journal of Pharmacology and Experimental Therapeutics. 191(1):82-91, 1974.

The hypothesis that inhibition of firing in the nigro-neostriatal dopamine system is followed by an immediate and rapid increase in the rate of dopamine synthesis in the neostriatum was examined using male rats. A similar phenomenon is not observed in the norepinephrine or serotonin systems in brain. The increase in synthesis appears to take place at the tyrosine hydroxylase step. Although the synthesis of dopamine returns to normal after dopamine levels have been increased, the elevated dopamine levels do not have a further inhibitory effect on tyrosine hydroxylase activity. Pretreatment with dopamine agonists such as 1-(2-pyrimidyl)-piperonyl-piperazine (ET495) or apomorphine prevents the increase in dopamine synthesis normally observed after inhibition of impulse flow. One possible explanation for these phenomena may be found in the hypothesis that a presynaptic receptor on the dopamine terminal may be involved in the regulation of dopamine synthesis and storage. 46 references. (Author abstract)

202665 Enna, S. J.; Da Prada, M.; Pletscher, A. Department of Pharmacology and Experimental Therapeutics, Johns Hopkins University, School of Medicine, Baltimore, MD 21205 **Subcellular distribution of reserpine in blood platelets: evidence for multiple pools.** Journal of Pharmacology and Experimental Therapeutics. 191(1):164-171, 1974.

Subcellular distribution of reserpine in rabbit blood platelets was examined. After i.v. administration, 3H-reserpine accumulated in blood platelets showed an initial rapid decrease between 0.5and 6 hours. The 3H-reserpine content remained virtually constant through day 5, followed by another marked diminution which was accompanied by a gradual recovery of the 5-hydroxytryptamine (5-HT). The 5-HT organelles isolated from the platelets showed a similar time course of the 3H-reserpine disappearance, except that no initial rapid decrease occurred. Pretreatment with unlabeled reserpine interfered with the accumulation of 3H-reserpine in whole platelets and 5-HT organelles, whereas administration of the unlabeled after the labeled drug did not diminish the level of radioactivity. Imipramine, given shortly before 3H-reserpine, inhibited the accumulation of the labeled drug in the whole platelets during the first 0.5hour, but not at later times. It is concluded that some reserpine initially accumulates reversibly outside the 5-HT granules, but that the bulk of the drug is permanently and irreversibly bound to 5-HT granules as well as to other sites in platelets and probably megakaryocytes. 24 references. (Author abstract modified)

202715 Kellogg, Carol; Wennerstrom, Gabriella. Department of Psychology, University of Rochester, Rochester, NY 14627 **An ontogenic study on the effect of catecholamine receptor-stimulating agents on the turnover of noradrenaline and dopamine in the brain.** Brain Research (Amsterdam). 79(3):451-464, 1974.

The ontogeny of catecholamine containing neurons and receptors in the brain sensitive to catecholamines was studied by examining the decrease of dopamine (DA) and noradrenaline (NA) following synthesis inhibition, and the ability of catecholamine receptor stimulating agents to attenuate the decrease. Analysis was performed in rats at 4, 14 and 28 days postnatal age. NA and DA synthesis was inhibited by alpha-methyl-p-tyrosine methyl ester (MT), and apomorphine and clonidine were utilized as DA and NA receptor stimulating agents, respectively, and were injected 30 min prior to administration of MT. The data obtained suggest that functional NA containing neurons are present in the cortex and brainstem by 4 days of age, with feedback control over turnover of NA from effective postsynaptic receptors developing concurrently. Functional NA containing neurons and receptors were not apparent in the diencephalon, according to criteria used in the present study, until 28 days. Functional DA containing neurons appeared present in the striatum and diencephalon by 4 days of age, but ontogeny of the DA receptors and/or feedback control from effective postsynaptic receptors appeared to vary. These results were interpreted to suggest that the numerous mechanisms controlling the release of DA may be developing at different times. 23 references. (Author abstract modified)

202716 Zivkovic, Branimir; Guidotti, Alessandro. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Changes of kinetic constant of striatal tyrosine hydroxylase elicited by neuroleptics that impair the function of dopamine receptors.** Brain Research (Amsterdam). 79(3):505-509, 1974.

The hypothesis that the change in the kinetic properties of striatal tyrosine hydroxylase (TH) is mediated via the blockade of dopaminergic receptors was tested in rats. Apomorphine did not change the kinetic properties of striatal TH, but antagonized the effects of neuroleptics on the Km for the pteridine cofactor. It is suggested that the kinetic properties of striatal TH may depend on the functional state of the dopaminergic receptors. It is concluded that the allosteric change of TH after treatment with neuroleptic drugs may be a molecular base for the increased turnover of striatal dopamine. 22 references.

202717 Mao, C. C.; Guidotti, A.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **The regulation of cyclic guanosine monophosphate in rat cerebellum: possible involvement of putative amino acid neurotransmitters.** Brain Research (Amsterdam). 79(3):510-514, 1974.

The relationships between cyclic guanosine-30,50-monophosphate (cGMP) concentration and neuronal mechanisms which utilize gamma-aminobutyric acid (GABA), glycine and glutamic acid as transmitters were examined in

rats. Picrotoxin, a GABA receptor blocker, and isonicotinic acid hydrazide which decreases the endogenous GABA content of cerebellum, increased cGMP concentrations. Strychnine was without effect. It is suggested that glycine may reduce the firing rate of GABA neurons resulting in a disinhibition of the inhibition exerted by GABA on the cGMP system. Experiments with harmaline indicate that the cGMP system of cerebellum may be stimulated when firing Purkinje cells is enhanced by excitation of the climbing fibers. It is suggested that glutamate is released from climbing fibers and acts on Purkinje cell receptors. 18 references.

202718 Bramwell, G. J. Department of Pharmacology, Medical School, Birmingham B15 2TJ, England **Factors affecting the activity of 5-HT-containing neurones.** Brain Research (Amsterdam). 79(3):515-519, 1974.

The hypothesis that there is a negative feedback system whereby the activity of 5-hydroxtryptamine (5-HT) neurons is self-regulating and that this system is influenced by drugs was tested. p-Chlorophenylalanine and p-chloromethylamphetamine did not increase the basal firing rate of 5-HT containing neurons. It is suggested that the drugs reduce raphe unit firing rate through other mechanisms. 28 references.

202719 Garey, Richard E.; Heath, Robert G. Department of Psychiatry and Neurology, Tulane University School of Medicine, New Orleans, LA 70112 **Uptake of catecholamines by human synaptosomes.** Brain Research (Amsterdam). 79(3):520-523, 1974.

The existence of an uptake mechanism which will actively incorporate tritiated norepinephrine (NE) and tritiated dopamine (DA) into synaptosomes derived from human brain tissue is reported. Results indicate that the Km's determined for human brain tissue obtained up to 8 hr after death were representative of Km values that would be obtained from human brain at 1 hr postmortem. Decreases observed in Vmax values for both norepinephrine and dopamine in rat synaptosomes were probably due to degeneration of a portion of the nerve endings. Synaptosomes derived from the subcortical regions of human brain, the dorsal caudate nucleus and the septal region retained active high affinity uptake for accumulation of the putative catecholaminergic transmitters, norepinephrine and dopamine. This mechanism was consistent with Michaelis-Menten type kinetics; it was temperature dependent and remained functional for at least 7 hrs after death. 20 references.

202723 Rosloff, Barry N.; Davis, John M. Department of Pharmacology, Vanderbilt University, Nashville, TN 37203 **Effect of iprindole on norepinephrine turnover and transport.** Psychopharmacologia (Berlin). 40(1):53-64, 1974.

The effects of iprindole, an antidepressant drug clinically similar to other tricyclic antidepressants, on norepinephrine turnover and transport in rats were examined. Such treatment did not alter the rate of decline of the log of brain norepinephrine levels after norepinephrine synthesis inhibition with alpha-methyltyrosine methyl ester. In addition, a single dose of iprindole did not significantly alter uptake of intracisternally administered H3-norepinephrine or the amount of H3-normetanephrine formed from such administration. Furthermore, iprindole added in vitro showed very low potency in blocking the uptake of labeled norepinephrine, metaraminol, serotonin, and dopamine into crude synaptosomal preparations. The bearing of these findings on the hypothesized mechanism of action of the tricyclic antidepressants, which affect all of the above parameters, is discussed. 47 references. (Author abstract)

202765 Babbini, M.; Torrielli, M. V.; Gaiardi, M.; Bartoletti, M.; De Marchi, F. Istituto di Farmacologia, Universita di Bologna, Via Irnerio 48, I-40126 Bologna, Italy **Central effects of three fluorinated benzodiazepines in comparison with diazepam.** Pharmacology (Basel). 12(2):74-83, 1974.

The central effects of the 5-(o-fluorophenyl)-3-hydroxybenzodiazepines SAS-643, SAS-646, and Ro-7-5205 were investigated and compared with those of diazepam. It was found that, in rats, these drugs have a pharmacological profile very close to that of diazepam. They possessed a high antimetrazol activity, a muscle relaxant effect and a depressive action upon exploratory behavior. They facilitated behavior suppressed by punishment and caused a synchronization of the electroencephalogram pattern. With regard to the relative potencies of the compounds, SAS-646 was found to be the most potent drug by far; it was 4-10 times more potent than diazepam, while SAS-643 was equipotent to the latter. This suggests the usefulness of the new compounds for clinical use. 16 references. (Author abstract modified)

202767 Lullmann-Rauch, Renate. Department of Anatomy, University of Kiel, Olshausenstrasse, D-2300 Kiel, Germany **Lipidosis-like alterations in spinal cord and cerebellar cortex of rats treated with chlorphentermine or tricyclic antidepressants.** Acta Neuropathologica (Berlin). 29(3):237-249, 1974.

Prolonged treatment of rats with the anorectic drug chlorphentermine or the tricyclic antidepressants iprindole and 1-chloro-amitriptyline caused the formation of numerous cytoplasmic inclusions in nerve cells of the cervical spinal cord and cerebellar cortex. The antidepressant drugs clomipramine, amitriptyline and noxiptiline had only weak or no effects. The abnormal, membrane bound inclusions consisted either of parallel or concentrically arranged lamellae, or they exhibited crystalloid or reticular internal patterns. The alterations correspond to previous observations on extraneural tissues of drug-treated animals. According to a proposed concept, the findings are interpreted to reflect a drug-induced lipidosis. 36 references. (Author abstract)

202771 Grabowska, Maria. Polish Academy of Sciences, Institute of Pharmacology, 31-344 Krakow, Poland **Influence of midbrain raphe lesion on some pharmacological and biochemical effects of apomorphine in rats.** Psychopharmacologia (Berlin). 39(4):315-322, 1974.

The influence of apomorphine on body temperature, motor activity and forebrain content of serotonin and 5-hydroxyindoleacetic acid in midbrain raphe lesioned rats was investigated. Apomorphine elevates the brain concentration of serotonin and its metabolite and promotes hypothermia in normal and in sham lesioned rats but it does not produce these biochemical effects and attenuates hypothermia in rats with lesions of the midbrain raphe nuclei. In the lesioned subjects, apomorphine stimulates the locomotor activity more strongly. The results confirm the hypothesis concerning the role of serotonin in the locomotor stimulation and hypothermia induced by apomorphine in rats. 24 references. (Author abstract)

202775 Howes, J.; Osgood, P. Sheehan Institute, 767B Concord Avenue, Cambridge, MA 02138 **The effect of delta9-tetrahydrocannabinol on the uptake and release of 14C-dopamine from crude striatal synaptosomal preparations.** Neuropharmacology (Oxford). 13(12):1109-1114, 1974.

The question of how delta9-tetrahydrocannabinol (THC) and a water-soluble derivative (compound I) may alter the uptake and release of dopamine in preparations derived from the cen-

tral nervous system and to try to account for the interactions reported with amphetamine and pemoline was examined. THC and a water-soluble ester derivative (compound I) caused a concentration related decrease in the uptake of 14C-dopamine into crude synaptosomal preparations derived from mouse striata. Both were less potent than amphetamine in this preparation. In the presence of amphetamine the THC was unaffected. The IC50 is the concentration of drug in the medium which will inhibit the uptake of 14C-dopamine into the synaptosomes by 50%. In the presence of THC, the dose response curve to amphetamine was shifted to the right and the IC50 of amphetamine was increased. Tetrahydrocannabinol and compound I increased the release of 14C-dopamine from preparations preincubated with 14C-dopamine. The effect was small but significant. The effects of amphetamine and THC combined were additive on this system. The mode of action of THC with regard to the dopaminergic system of the striatum is discussed. 25 references. (Author abstract modified)

202777 Frazer, A.; Pandey, G.; Mendels, J.; Neeley, S.; Kane, M.; Hess, Marilyn E. VA Hospital, Philadelphia, PA 19104 **The effect of tri-iodothyronine in combination with imipramine on (3H)-cyclic AMP production in slices of rat cerebral cortex.** Neuropsychopharmacology (Oxford). 13(12):1131-1140, 1974.

Tri-iodothyronine (T3) was administered to rats, alone or in combination with imipramine for 5 days. The net synthesis of (3H)-cyclic adenosine monophosphate (cAMP) in cerebral cortex slices of animals so treated and control rats was then measured. The dose-dependent stimulation of (3H)-iodothyronine treatment had no effect on the enhanced net synthesis of (3H)-cyclic AMP produced by NE. In cortex slices of rats given both T3 and imipramine, NE produced less stimulation of (3H)-cyclic AMP than in control rats. The magnitude of this inhibitory effect was less than that observed in animals treated with imipramine alone. In vitro addition of imipramine to the cortex slice preparation reduced the stimulation of (3H)-cyclic AMP caused by NE; treatment of rats with T3 did not modify this inhibitory effect of imipramine in vitro. Isoproterenol produced significantly less stimulation of (3H)-cyclic AMP net synthesis than did NE; imipramine added in vitro had no effect on the stimulation produced by isoproterenol. It is concluded that the reason for the enhanced clinical effect of imipramine when given together with T3 is not due to the hormone exaggerating the effect of the antidepressant on NE stimulated adenylate cyclase. 58 references. (Author abstract modified)

202778 Bieger, D. University of Illinois, College of Medicine at Urbana-Champaign, 1205 W. California St., Urbana, IL 61801 **Influence of striatal dopamine receptor blockade on a bulbar motor reaction.** Neuropharmacology (Oxford). 13(12):1141-1152, 1974.

An oropharyngeal myocloniform response of rats, anesthetized with urethane, to the administration of L-DOPA and 5-hydroxytryptophan (5-HTP) was studied in an attempt to differentiate its dopaminergic and serotoninergic components. Bilateral intrastriatal microinjections of chlorpromazine (CPZ) effected decreases of the myocloniform response (twitch frequency) to systemic or intracarotid L-DOPA injections, but had little effect on responses to 5-HTP. When injected into the striatum, haloperidol exhibited a slightly stronger antagonism towards L-DOPA than did CPZ. Upon intravenous administration, both neuroleptic drugs also antagonized the myoclonigenic action of L-DOPA, CPZ being approximately twice as potent as haloperidol. Electrical stimulation of the ventral tegmentum through an electrode inserted into the substantia nigra or its rostrodorsal perimeter was effective in eliciting myocloniform twitching of oropharyngeal musculature. The frequency component of this response was sensitive neither to ipsilateral intrastriatal injections of CPZ or haloperidol, nor to acute ipsilateral prethalamic hemitransection of the brain, but could be inhibited by intravenous administration of haloperidol. 26 references. (Author abstract modified)

202782 Freeman, J. J.; Sulser, F. Department of Pharmacology, UCLA School of Medicine, Los Angeles, CA 90024 **Formation of p-hydroxynorephedrine in brain following intraventricular administration of p-hydroxyamphetamine.** Neuropharmacology (Oxford). 13(12):1187-1190, 1974.

p-Hydroxynorephedrine (PHN) accumulated in brain tissue following the intraventricular administration of tracer amounts of p-hydroxyamphetamine (POH). Only small amounts of radioactivity were detected in the POH and PHN fractions and no accumulation of PHN occurred following the intraventricular administration of (+)-amphetamine. These results support the view that (+)-amphetamine following its systemic administration is p-hydroxylated in the periphery to POH which then crosses the blood-brain barrier, is taken up by noradrenergic neurons in brain and converted to PHN. 12 references. (Author abstract)

202795 Otten, U.; Mueller, R. A.; Thoenen, H. Institut fur Pharmakologie, Biozentrum der Universitat Basel, Switzerland **Evidence against a causal relationship between increase in c-AMP and induction of tyrosine hydroxylase in the rat adrenal medulla.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 285(3):233-242, 1974.

To determine whether the reserpine mediated changes in adrenomedullary cyclic adenosine monophosphate (c-AMP) result from alpha- or beta-adrenergic activation of adenylate cyclase by catecholamines liberated from adrenal chromaffin cells, the changes and subsequent induction of tyrosine hydroxylase (TH) were examined. The reserpine mediated increase in c-AMP was blocked by neither alpha- nor beta-adrenergic blocking agents. However, propranolol abolished the increase in c-AMP by a mechanism which is not related to the beta blocking properties of this drug. Although propranolol abolished the reserpine mediated increase in c-AMP, it did not interfere with the subsequent TH induction. Administration of aminophylline together with reserpine produced a larger and more prolonged increase in c-AMP in denervated adrenals than reserpine alone in intact glands. Denervation prevented TH induction in spite of the more extensive increase in c-AMP in the adrenal medulla after the combined treatment. It is concluded that there is no causal relationship between the overall increase in c-AMP in the adrenal medulla and the subsequent TH induction. 22 references. (Author abstract modified)

202796 Zetler, G.; Back, G.; Iven, H. Institut fur Pharmakologie der Medizinischen Hochschule, D-2400 Lubeck, Germany **Pharmacokinetics in the rat of the hallucinogenic alkaloids harmine and harmaline.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 285(3):273-292, 1974.

The pharmacokinetics of harmine and harmaline were examined in the cat. Highest concentrations occurred for harmine in the lung and for harmaline in the kidney. The uptake into brain was for harmaline slower than for harmine. The rate of elimination was in general smaller for harmaline than for harmine. Harmaline was excreted into chymus and urine to a greater extent than harmine. The binding to proteins of rat

plasma was 94.5% for harmine and 52% for harmaline. The extent of tissue binding and the rate of its development were different for both drugs. The duration of tremor and the strength and decline of bradycardia were determined to compare the distribution of the drugs with their effects. 38 references. (Author abstract modified)

202799 Toda, Noboru; Hojo, Masakazu; Sakae, Koichiro; Usui, Hachiro. Department of Pharmacology, Faculty of Medicine, Kyoto University, Kyoto, Japan **Effects of 5-hydroxyindoleacetic acid on isolated canine cerebral arteries.** Japanese Journal of Pharmacology (Kyoto). 24(4):642-644, 1974.

The effects of 5-hydroxyindoleacetic acid (5-HIAA) on isolated canine cerebral arteries were examined. Serotonin (5-HT) caused a dose-dependent increase in tension while 5-HIAA acid elicited relaxation which was not inhibited by propranolol, atropine and ouabain. It is suggested that beta-adrenergic, cholinergic and electrogenic sodium pump mechanisms are not involved in the genesis of the relaxation. Results indicate that the deaminated metabolite of 5-HT, 5-HIAA, showed neither serotonin-like or antiserotonin action while, in contrast, a metabolite of serotonin in which the indole ring was open possessed both serotonin-like and antiserotonin actions. 8 references.

202800 Furukawa, Tatsuo; Kushiku, Kazushi; Kawagoe, Tetsumi. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Fukuoka University, Fukuoka, Japan **Species differences in antagonistic effect of morphine against depressor response to dopamine.** Japanese Journal of Pharmacology (Kyoto). 24(4):635-638, 1974.

Species differences in antagonistic effect of morphine against depressor response to dopamine, determined by the minimum level of blood pressure attained, were observed in dogs, cats and rabbits. A depressor response to dopamine after alpha-adrenergic blockade was eliminated by morphine in cats, but potentiated in dogs. The response to dopamine after repeated injections of ephedrine was potentiated by morphine both in cats and dogs. Without pretreatment in rabbits, the response to dopamine was diminished by morphine. It thus appears that species difference is considerable regarding antagonism of morphine to dopamine in blood pressure responses. 12 references. (Author abstract)

202801 Yasuhara, Hajime Department of Pharmacology, School of Medicine, Showa University, Shinagawa-Ku, Tokyo, Japan **Studies on monoamine oxidase (report XXIV) effect of harmine on monoamine oxidase.** Japanese Journal of Pharmacology (Kyoto). 24(4):523-533, 1974.

Using beef brain and liver mitochondria, the effects of several inhibitors on the oxidation of serotonin and tyramine were studied. Mitochondrial monoamine oxidase (MAO) of beef brain showed pH optima of 8.8with serotonin and 8.0with tyramine. Pheniprazine had similar effects on the oxidations of serotonin and tyramine by brain MAO at pH 7.4and pH 8.5. Amphetamine inhibited serotonin oxidation much more than tyramine oxidation by brain MAO both a pH 7.4and pH 8.5. Harmine selectively inhibited serotonin oxidation by brain MAO at pH 7.4. It inhibited serotonin oxidation by brain MAO competitively and tyramine oxidation uncompetitively. The effect of harmine on MAO of brain mitochondria differed markedly before and after heat treatment. These results suggest that there are at least two types of MAO in beef brain mitochondria: one heat labile, with low affinity for harmine, and the other rather heat stable, with high affinity for harmine. Harmine inhibited liver MAO only very slightly with either serotonin or tyramine as substrate. 30 references. (Author abstract modified)

202804 Fukuda, Hideomi; Ito, Tsugutaka; Hashimoto, Satoe; Kudo, Yoshihisa. Department of Chemical Pharmacology, Nagoya City University, Tanabe-dori, Mizuho-Ku, Nagoya, Japan **Rigidity in rats due to anemic decerebration and the effect of chlorpromazine.** Japanese Journal of Pharmacology (Kyoto). 24(5):810-813, 1974.

The effect of chlorpromazine on rigidity in rats due to anemic decerebration was examined. Rigidity developed within 30 min after ligation of the common carotid arteries and cauterization of the basilar artery. Results indicate that the function of the gamma loop has little or no effect on the occurrence of the anemic decerebrate rigidity. Chlorpromazine exerted no effect on anemic rigidity but the effect was much stronger on intercollicular decerebrate rigidity. 9 references.

202805 Starke, K.; Montel, H. Pharmakologisches Institut, Universitats-Klinikum Essen, Germany **Alpha-receptor-mediated modulation of transmitter release from central noradrenergic neurones.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 279(1):53-60, 1973.

Slices of rat cerebral cortex were preincubated with 10 micromoles of 3H-noradrenaline, and the outflow of tritium was determined. Oxymetazoline, phentolamine and cocaine did not change the spontaneous efflux. The overflow of tritium evoked by electrical field stimulation was decreased by oxymetazoline, and enhanced by phentolamine, phenoxybenzamine, and cocaine. Oxymetazoline did not counteract the increase of the stimulation-induced overflow caused by cocaine, but strongly antagonized the increase caused by phentolamine and phenoxybenzamine. When the stimulation-induced overflow was large under control conditions (high frequency of stimulation, addition of cocaine), the inhibitory effect of oxymetazoline was diminished. The results indicate that an alpha-receptor mediated feedback control of noradrenaline release, previously demonstrated in postganglionic sympathetic nerves, also operates in central noradrenergic neurones. 17 references. (Author abstract)

202807 Schacht, Ulrich; Heptner, Wolfgang. Farbwerke Hoechst AG, vormals Meister Lucius and Bruning, Frankfurt(M)-Hochst, Germany **Effect of nomifensine (HOE 984), a new antidepressant, on uptake of noradrenaline and serotonin and on release of noradrenaline in rat brain synaptosomes.** Biochemical Pharmacology (Oxford). 23(24):3413-3422, 1974.

The effects of nomifensine (8-amino-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline hydrogen maleate) on noradrenalin (NA) and serotonin (5-HT) uptake by crude synaptosome preparations from both whole rat brain and from hypothalamus were studied and compared with those of several tricyclic antidepressants and D-amphetamine. Nomifensine inhibition of NA uptake by synaptosomal fractions from rat hypothalamus was similar to that of nortriptyline and protriptyline. In contrast to tricyclic antidepressants, nomifensine was found to be a powerful inhibitor of NA uptake in synaptosomes obtained from whole brain. Nomifensine had only a moderate effect on 5-HT accumulation, comparable with that of desipramine. The inhibition of uptake of both NA and 5-HT by nomifensine was of a competitive type. It is suggested that the centrally stimulating component of nomifensine, which is lacking in most thymoleptic drugs, is based upon its strong inhibition of catecholamine reuptake into noradrenergic as well as dopaminergic nerve endings. Nomifensine has no releasing effects on the efflux of NA

from rat brain synaptosomes, thus differing clearly from D-amphetamine and other indirectly acting sympathicomimetic agents. 37 references. (Author abstract modified)

203028 Lukes, James John. University of Connecticut, Storrs, CT **Central nervous system carbonic anhydrase inhibitors. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-21795 HC$12.50 MF$4.00 161 p.

The design and synthesis of a series of compounds related to the carbonic anhydrase inhibitor, methazolamide, were studied. The capacity of such derivatives to inhibit carbonic anhydrase of brain in vitro and in vivo was examined. Each of the synthesized compounds possessed a pKa which was greater than that of the reference compound methazolamide. Utilizing a micromethod colorimetric scheme, the entire series of compounds demonstrated the ability to inhibit brain carbonic anhydrase in vitro. The majority of the test compounds possessed in vitro inhibitory activity on brain carbonic anhydrase and in vivo capacity to control convulsive seizures induced by pentylenetetrazole. A number of the compounds in this series possess a relative capacity to selectively localize within the brain and to inhibit the activity of carbonic anhydrase enzyme contained in the glial cellular elements. (Journal abstract modified)

203032 Blumberg, Jeffrey Bernard. Vanderbuilt University, Nashville, TN **The role of cerebral cyclic AMP in the action of psychotropic drugs: in vivo and in vitro studies. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-22162 HC$12.50 MF$4.00 258 p.

In vivo and in vitro studies were examined to demonstrate the role of cerebral cyclic AMP in the action of psychotropic drugs. CNS depression induced by pentobarbital was associated with a decrease in levels of cyclic AMP while CNS stimulation caused by methylphenidate elicited no change in basal levels of cyclic AMP. Norepinephrine was found to increase the in vitro accumulation of cyclic AMP in slices from cerebral cortex of rats. At concentrations equimolar with norepinephrine, phenothiazines and butyrophenones, as well as pimozide and clozapine, antagonized the selective norepinephrine induced increase in cyclic AMP. These data suggest that the norepinephrine sensitive cyclic AMP system in the limbic forebrain may be implicated in the mode of action of antipsychotics. (Journal abstract modified)

203033 Gay, Michael Howard. Washington University, St. Louis, MO **Effects of phenobarbital on electrocorticogram and activity, on regional CNS energy metabolism, and on presynaptic events in cerebral cortex and brainstem. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-22515 HC$12.50 MF$4.00 152 p.

A simple and flexible system for simultaneously recording electrocorticogram (ECoG) and motor activity in unrestrained mice was developed to investigate the effects of phenobarbital on these parameters. Alterations in bipolar ECoG and motor activity of mice induced by phenobarbital are very similar to those described for other species. In a second study, effects of the drug on regional CNS energy metabolism were determined in mice during maximal excitation and during deep depression induced by phenobarbital. During excitation, neural activity was higher than control values in brainstem, lower in hippocampus, and unchanged in the other regions. During deep depression, neural activity was greatly depressed in every region except brainstem. A final study investigated presynaptic actions of phenobarbital in isolated nerve terminals from rabbit cerebral cortex and brainstem. The most significant findings were that phenobarbital blocked both K+ stimulated Ca++ uptake and K+ induced depletion of synaptic vesicles in synaptosomes isolated from brainstem but not in those from cerebral cortex. (Journal abstract modified)

203034 Morgan, James Philip. University of Cincinnati, Cincinnati, OH **Cardiovascular and autonomic effects of chlorpromazine. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-22716 HC$12.50 MF$4.00 182 p.

The effects of chlorpromazine HCl (CPZ) on the cardiovascular and autonomic nervous systems of chronically treated dogs were investigated. Chronic administration of oral CPZ produced hypotension in normotensive, anesthetized dogs. The hypotension persisted for at least 28 days. Results indicate that CPZ, or one of its congeners, may be useful as an antihypertensive agent, particularly in psychiatric patients who are also hypertensive. The differential blocking effect of CPZ provides a new approach to the study of drug-receptor interactions. (Journal abstract modified)

203573 Segal, Menahem; Landis, Story C. Laboratory of Neuropharmacology, Special Mental Health Research Division, IRP, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Afferents to the septal area of the rat studied with the method of retrograde axonal transport of horseradish peroxidase.** Brain Research (Amsterdam). 82(2):263-268, 1974.

Afferents to the septal area of the rat studied with the method of retrograde axonal transport of horseradish peroxidase (HRP) are reported. HRP was injected into the septal areas of 18 rats and the animals were examined 24 h later. The only telencephalic structure that contained labeled cells was the anterior hippocampus (HPC), just rostral to the genu of the corpus callosum. No labeled cells were found elsewhere in the HPC. Labeled cells were present in the periventricular area of the hypothalamus (HTH) extending from the level of the ventromedial HTH to the mammillary bodies and were concentrated in the dorsal periventricular area mainly at the dorsal aspect of the third ventricle. Labeled neurons which might be the source of dopamine-containing fibers in the septum were scattered in the anterior extent of the ventral tegmental area and just dorsal to the interpendicular nucleus. Many labeled cells were observed in the median raphe along its entire antero-posterior extent. Results are discussed. 21 references.

203580 Fuller, Ray W.; Perry, Kenneth W. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Long-lasting depletion of brain serotonin by 4-chloroamphetamine in guinea pigs.** Brain Research (Amsterdam). 82(2):383-385, 1974.

A study to determine if 4-chloroamphetamine produces a long-lasting depletion of brain serotonin in guinea-pigs is reported. Male animals were injected i.p. with the drug and killed at 6 h, 24 h or 1 week after injection. Results show that the depletion of brain serotonin by 4-chloroamphetamine is not species specific and is as long-lasting in the guinea-pig as it is in the rat. The knowledge that in the guinea pig as in the rat a single injection of the drug produces chronic-pig lowering of brain serotonin may be useful in pharmacologic manipulation of brain serotonin for functional studies. 5 references. (Author abstract modified)

203885 Goetz, Christopher; Klawans, Harold L. Division of Neurology, Michael Reese Medical Center, Chicago, IL 60616

Studies on the interaction of reserpine, d-amphetamine, apomorphine and 5-hydroxytryptophan. Acta Pharmacologica et Toxicologica (Kobenhavn). 35(2):119-130, 1974.

The effect of reserpine-on dopamine related d-amphetamine and apomorphine-induced stereotyped behaviors and serotonin-related myoclonic behavior was studied. Reserpine pretreatment potentiated amephetamine-induced stereotyped behavior, apomorphine-induced stereotyped behavior and 5-hydroxytryptophan-induced myoclonic behavior. The possibility that this was related to the influence of reserpine on the behaviorally-active monoamine pools is discussed. 5-Hydroxytryptophan in small amounts was found to inhibit amphetamine-induced stereotyped behavior in reserpine-pretreated guinea pigs. d-Amphetamine appeared to potentiate 5-hydroxytryptophan myoclonic behavior and this potentiation was further increased by reserpine. 5-Hydroxytryptophan did not inhibit apomorphine-induced stereotyped behavior in reserpinized animals. These results are discussed in relation to the influence of reserpine on the balance of active neurotransmitters within the brain. 19 references. (Author abstract modified)

204183 Pieri, Lorenzo; Pieri, Margherita; Haefely, Willy. Department of Experimental Medicine, F. Hoffman-La Roche and Co., Ltd., Grenzacherstrasse 124, Basel, Switzerland, CH4002 **LSD as an agonist of dopamine receptors in the striatum.** Nature (London). 252(5484):586-588, 1974.

Lysergic acid diethylamide (LSD) is discussed as a potent agonist of dopamine receptors in the striatum, based on studies using a modification of the rotational model proposed by Understedt. It was found that in rats with the nigro-striatal dopamine system lesioned unilaterally by injection into the medial forebrain bundle of two different neurotoxic agents, LSD induced circling towards the intact side exactly as does apomorphine. The activation of striatal dopamine receptors is concluded to not be the only important central effect of LSD, since its overall behavioral effects differ considerably from those of agents believed to be fairly pure agonists of dopamine receptors. The possible importance of the dopaminergic component of the action of LSD for its hallucinogenic effect has yet to be demonstrated. 23 references.

204184 von Hungen, Kern; Roberts, Sidney; Hill, Diane F. Department of Biological Chemistry, School of Medicine, University of California Center for the Health Sciences, Los Angeles, CA 90024 **LSD as an agonist and antagonist at central dopamine receptors.** Nature (London). 252(5484):588-589, 1974.

Evidence is reported that D-lysergic acid diethylamine (D-LSD) may act as both an agonist and an antagonist at dopamine receptors in the brain. Brains were obtained from young, adult male rats of an inbred Sprague Dawley strain. Particulate fractions were prepared from cerebral cortex or corpus striatum. In relatively low concentration (10 micromoles), D-LSD completely blocked the stimulation of cerebral adenyl cyclase activity by a combination of 10 micromoles noradrenaline and 10 micromoles dopamine. D-LSD also inhibited the adenyl cyclase response to noradrenaline or dopamine in particulate preparations from the rat hippocampus. By itself, D-LSD tended to increase adenyl cyclase activity in the cerebral and hippocampal preparations, although the effect was small and not always significant. The findings indicate that D-LSD is capable of blocking the interaction of noradrenaline, dopamine and serotonin with their respective receptors in various regions of rat brain. The investigations suggest that the hallucinogenic actions of D-LSD may be due to complex agonist and antagonist actions of this drug at central receptors for the several neurotransmitter monoamines. 19 references.

204185 Archibald, J. T.; White, Thomas D. Department of Pharmacology, Dalhousie University, Halifax, Nova Scotia, Canada **Rapid reversal of internal Na+ and K+ contents of synaptosomes by ouabain.** Nature (London). 252(5484):595-596, 1974.

Evidence is reported that ouabain reverses the normal Na+ and K+ contents of synaptosomes within 1 minute of exposure to the drug, indicating that presynaptic terminals might be particularly sensitive to drugs which influence Na+ pump activity. Synaptosomes were prepared from the brains of two male Wistar rats and isolated on sucrose density gradients before being finally resuspended with 0.5ml of ice cold 0.32 M sucrose. One mM ouabain caused a significant reduction in synaptosomal K+ content at 30 sec with a maximal effect by 1 min. Synaptosomes gained Na+ during incubation but ouabain increased further the Na+ content after 1 min. with a maximal effect achieved after 3 min. The results indicate the ouabain can very quickly reverse the Na+ and K+ contents of synaptosomes. 18 references.

204220 Feger, J.; Boulu, R.; Rossignol, P. 4, Avenue Gordon-Bennett, Paris 16eme, France /**The blink reflex to light: its course and its facilitation by reserpine.**/ Le reflexe de clignement a la lumiere: etude de son trajet et de sa facilitation par la reserpine. Electroencephalography and Clinical Neurophysiology (Amsterdam). 32(3):247-258, 1972.

The pathway of the blink reflex to light, or the retino-palpebral reflex, has been studied. Beginning in retinal cells, its path follows the optic tract, includes multiple relays in the lateral geniculate body (LGB) and goes on by a pathway which directly and without forming synapses connects the LGB and facial nucleus. Stimulation of the superior colliculus or the pretectal area does not evoke a response in the facial nerve. The destruction of these structures does not suppress the reflex. These results make it possible to limit the diencephalic relay area to the LGB. Facilitation of the retino-palpebral reflex appear in the cat after administration of reserpine. The area where this facilitation occurs was localized in the LGB; facilitatory action at the facial nucleus can be rejected; facilitation does not arise from an action of reserpine on retinal adrenergic termination. This drug provokes a decrease in amplitude of the potentials in the optic tract after light stimulation. The response in the facial nerve after electrical stimulation of the optic tract is considerably increased under reserpine. 56 references. (Author abstract modified)

204339 Jobe, P. C.; Stull, R. E.; Geiger, P. F. Division of Pharmacology and Therapeutics, Louisiana State University Medical Center, Shreveport, LA 71101 **The relative significance of norepinephrine dopamine and 5-hydroxytryptamine in the electroshock seizure in the rat.** Neuropharmacology (Oxford). 13(10/11):961-968, 1974.

The effects of various treatments on brain norepinephrine (NE), dopamine (DA) and 5-hydroxytryptamine (5-HT) were compared to the effects of these same treatments on electroshock seizure (ES) intensity. The data indicate that depletion of all three biogenic amines by reserpine or the benzoquinolizine Ro 4-1284, enhances ES intensity and that treatments which protect against depletion of NE and/or DA antagonize ES enhancement. Protection of 5-HT stores against depletion does not protect against ES enhancement. Following depletion of all three amines by Ro 4-1284, subsequent repletion of NE and DA singly or in combination is sufficient to antagonize Ro 4-1284-induced ES enhancement. Repletion of DA stores alone did not antagonize Ro 4-1284 seizure enhancement in animals treated with pimozide, a central DA receptor

blocking agent. It appears that both NE and DA exert central nervous system inhibitory effects which limit the spread of the electroshock seizure discharge and consequently regulate intensity of ES. The data indicate that 5-HT does not play a significant role in the modulation process. 24 references. (Author abstract)

204340 Gerson, S.; Baldessarini, R. J.; Wheeler, S. C. Psychiatric Research Laboratories, Massachusetts General Hospital, Boston, MA 02114 **Biochemical effects of dihydroxylated tryptamines on central indoleamine neurones.** Neuropharmacology (Oxford). 13(10,11):987-1004, 1974.

Biochemical effects of dihydroxylated tryptamines on central indoleamine neurons were examined. Intracisternal 5,6-dihydroxytryptamine (5,6-DHT) was more selective than 5,7- or 6,7-DHT in damaging indoleamine neurons in the rat medulla-spinal cord. It reduced 5-hydroxytryptamine (5-HT) levels by more than 80% in spinal cord but less in other regions: 5-hydroxyindoleacetic acid (5-HIAA) was also decreased; tryptophan was unchanged. Unlike the other analogues, 5,6-DHT did not affect the levels, uptake or synthesis of catecholamines. Accumulation of 5-HT and 5-HIAA synthesized from [3H]-tryptophan 15 min after intracisternal injection was markedly reduced in medulla-spinal cord; synthesis of 5-HT from [14C]-tryptophan in P2 fractions in vitro was also decreased. High affinity uptake of tryptophan into spinal cord synaptosomes was decreased after 5,6-DHT-treatment. These data support the conclusion that 5,6-DHT causes selective degeneration of central indoleamine axons. 50 references. (Author abstract modified)

204386 Mezey, Esteban. Alcoholism Research Unit, Dept. of Medicine, Beltimore City Hospitals, Johns Hopkins Univ. School of Medicine, Baltimore, MD 21224 **Effect of phenobarbital administration on ethanol oxydizing enzymes and on rates of ethanol degradation.** Biochemical Pharmacology. 20(2):508-510, 1971.

Phenobarbital, an inducer of microsomal enzymes, was used in testing the activity of ethanol-oxidizing systems and the rates of ethanol disappearance from the blood. The drug was given to 24 male rats I.P. at a daily dose of 100mg/kg for 3 days to one group, and for 5 days to another. Phenobarbital administration resulted in significant increases in liver weight, microsomal protein concentration, aniline hydroxylase activity and cytochrome P-450, and the circulated total hepatic activities of the ethanol-oxidizing enzymes were increased. Total alcohol dehydrogenase increased 17% and microsomal ethanol-oxidizing system increased 40% over control values after 5 days of phenobarbital. Rates of ethanol disappearance from the blood were not significantly altered by phenobarbital. It was concluded that other than the absolute changes in ethanol-oxidizing enzymes regulate the rates of ethanol disappearance from the blood. 13 references.

204396 Estler, C.-J. Pharmakologisches Institut der Universitat Erlangen-Nurnberg, 852 Erlangen, Universitatsstr. 22, Germany /**The influence of antiadrenergic and antidopaminergic drugs on methamphetamine induced changes in motoric activity and cerebral glycogen content in mice.**/ Der Einfluss antiadrenerger und antidopaminerger Pharmaka auf die durch Methamphetamin verursachten Anderungen der motorischen Aktivitat und des zerebralen Glykogengehalts bei Mausen. Arzneimittel-Forschung (Aulendorf). 24(8):1087-1088, 1974.

The influence of antiadrenergic and antidopaminergic drugs on methamphetamine-induced changes in motor activity and cerebral glycogen content was examined in mice. Methamphetamine increased motor activity markedly and decreased cerebral glycogen content. Phenoxybenzamine diminished the motor excitation but not the decrease of the cerebral glycogen. Propranolol diminished the methamphetamine-induced hyperactivity and blocked completely the decrease of the glycogen content of the brain. P-Chlorophenylalanine prevented the depletion of the brain glycogen but had no uniform effect on the motility of the animals. Pimozide prevented both the decrease of the brain glycogen content and the hypermotility induced by methamphetamine. It appears that methamphetamine causes motor excitation and glycogen depletion in the brain by different and independent mechanisms. 8 references. (Journal abstract modified)

204483 Kirsten, Edward B.; Schoener, Eugene P.; Wang, S. C. Dept. of Pharmacology, College of Physicians and Surgeons, 630 West 168th St., New York, NY 10032 **Effects of d-amphetamine on single vestibular neurons.** Journal of Pharmacology and Experimental Therapeutics. 191(3):377-383, 1974.

The effects of d-amphetamine on single vestibular neurons of cats are discussed. Decerebrate or encephale isole cats were tested with controlled acceleratory motion in order to identify vestibular neurons activated by motion. The effects of d-amphetamine were studied on both neuronal unit activity and field potentials evoked by stimulation of a branch of the VIIIth nerve. Results indicate that d-amphetamine affects vestibular neurons through pathways other than those associated with primary afferent activity of the VIIIth cranial nerve. Central nervous system structures rostral to the inferior colliculus appear to be implicated in the d-amphetamine depression of vestibular firing. 35 references. (Author abstract modified)

204484 Hidaka, Hiroyoshi; Hara, Fumiko; Harada, Nobuo; Hashizume, Yoshio; Yano, Mituo. 713-1 Kamiya-cho Kasugai, Aichi-ken, 480-03, Japan **Selective inhibition of dopamine-beta-hydroxylase in the peripheral tissues by 5-dimethyldithiocarbamylpicolinic acid; its effect on stress-induced ulcer, ethanol-induced sleep and blood pressure.** Journal of Pharmacology and Experimental Therapeutics. 191(3):384-392, 1974.

An evaluation of the role of the central nervous system in both the depressor response and the prevention of stress-induced gastric ulcers after picolinic acid derivatives that inhibit dopamine-beta-hydroxylase (DBH) is presented. Administration of dimethyldithiocarbamylpicolinic acid (YP-279) caused selective reduction of peripheral norepinephrine (NE) biosynthesis and reduced the blood pressure of spontaneously hypertensive rats and normals but had no effect on brain NE biosynthesis. YP-279 did not affect stress-induced gastric ulcer or ethanol-induced sleeping time, both thought to be mediated in the central nervous system. Evidence that YP-279 is a selective inhibitor of peripheral dopamine-beta-hydroxylase is included. 5-Butylpicolinic acid, an analog of YP-279, and its derivatives exhibited all the effects of YP-279 as well as abilities to prevent stress induced gastric ulcers and to prolong ethanol-induced sleep. 20 references. (Author abstract modified)

204485 Cubeddu, L. X.; Barnes, E.; Weiner, N. Dept. of Pharmacology, Univ. of Colorado School of Medicine, 420 E. 9th Ave., Denver, CO 80220 **Release of norepinephrine and dopamine-beta-hydroxylase by nerve stimulation: II. Effects of papaverine.** Journal of Pharmacology and Experimental Therapeutics. 191(3):444-457, 1974.

The role of cyclic adenosine nucleotides on the regulation of adrenergic neurotransmission are evaluated in the cat. Papaverine, at a concentration which inhibits spleen phosphodiesterase activity (PDE), produced a marked increase in the nerve stimulation mediated overflow of norepinephrine (NE), tritium 3H-NE total 3H and dopamine-beta-hydroxylase (DBH) activity from islated, perfused cat spleen, prelabeled with 3H-NE. Results indicate that accumulation of 30,50-cyclic adenosine monophosphate subsequent to inhibition of PDE activity by papaverine probably accounts for only part of enhanced release of NE and DBH by nerve stimulation. Since the enhanced spontaneous release of 3H and the enhanced release of neurotransmitter associated with the nerve stimulation are highly correlated, the results suggest that a direct effect of papaverine on the synaptic vesicles and its effect on nerve stimulation mediated release of NE and DBH could be related. 35 references. (Author abstract modified)

204864 Bellin, Judith S.; Sorrentino, G. M. Dept. of Chemistry, Polytechnic Institute of New York, Brooklyn, NY 11201 **Activation of brain monoamine oxidase by some CNS depressants.** Research Communications in Chemical Pathology and Pharmacology. 9(4):673-680, 1974.

The effect of several known tranquilizers on monamine: oxygen oxidoreductase EC 1. 4. 3. 4 (MAO) in vitro was examined. In the presence of 0.25 mM serotonin reserpine, levallorphan, secobarbital, thiopental, barbital and morphine increase the deaminating catalysis of MAO from 15 to 48%. The activating effect of these compounds is correlated with extent of their physiological action. In contrast, the stimulant caffeine is a reversible competitive inhibitor of MAO. 17 references. (Author abstract modified)

204866 Osgood, P.; Howes, J. 767-B Concord Avenue, Cambridge, MA 02138 **Cannabinoid induced changes in mouse striatal homovanillic acid and dihydroxyphenylacetic acid: the effects of amphetamine and L-dopa.** Research Communications in Chemical Pathology and Pharmacology. 9(4):621-631, 1974.

Changes which occur in homovanillic acid (HVA) and dihydroxyphenylacetic acid (DOPAC) after treatment with delta9-tetrahydrocannabinol (delta9-THC) were studied. Delta9-THC alone did not significantly alter DOPAC or HVA. Delta9-THC did not significantly alter the amphetamine-induced reduction of striatal HVA; however, there was a significant reversal of the amphetamine-induced decrease in DOPAC. L-Dopa (200mg/kg ip) increased striatal DOPAC but not HVA. Delta9-THC increased the striatal levels of HVA and DOPAC in L-Dopa-treated animals. The effect of delta9-THC was dose-dependent and both DOPAC and HVA levels were increased to an equivalent extent. Delta9-THC appears to alter the disposition of dopamine intraneuronally without any effects on the enzymes involved in its metabolism. 30 references. (Author abstract modified)

205169 Beaulac-Baillargeon, L. Ecole de pharmacie, Universite Laval, Quebec, Canada /**A contribution to the study of mechanism of action of phenylbutazone: the influence of catecholamines on the antiinflamatory effect of phenylbutazone.**/ Contribution a l'etude du mecanisme d'action de la phenylbutazone: influence des catecholamines sur l'effet anti-inflammatoire de la phenylbutazone. Vie medicale au Canada francais (Quebec). 3(9):903-908, 1974.

The interaction between phenylbutazone and adrenergic stimulants and blockers was examined in male rats, using a technique of quantitative recovery of a dye linked to plasma proteins. It is suggested that the beta-receptors were responsible for the anti-inflammatory effect of phenylbutazone even when the beta-receptors were blocked by propranolol. It is hypothesized that phenylbutazone acts somewhere in the sequence after the cyclic-AMP synthesis, probably by inhibiting phosphodiesterase. 18 references. (Journal abstract modified)

205175 Ikeda, Ko. Dept. of Neurology and Psychiatry, Jikei University School of Medicine, Japan **Laboratory and clinical studies of lithium carbonate.** Tokyo Jikeikai Medical Journal (Tokyo). 88(6):1150-1178, 1973.

The distribution of lithium in the tissues of the rat CNS was investigated and the antimanic and therapeutic phase effects of lithium carbonate were assessed. The results show that adequate doses of the compound cause no significant difference in concentration between various CNS regions. Rats given a highly toxic dose developed signs of a cataleptoid state, and their various tissues tended to contain uniform concentrations of the element, whereas the skeletal muscles contained 169% of the mean level concentration. Lithium was effective in 35 out of 49 patients in the acute manic stage and long-term administration of lithium was efficacious in 13 of 16 cases. 63 references. (Journal abstract modified)

205433 Jonsson, John A. Psychiatric Research Center, University of Uppsala, Ulleraker Hospital, S-750 17 Uppsala, Sweden **Hydroxylation of amphetamine to para-hydroxyamphetamine by rat liver microsomes.** Biochemical Pharmacology (Oxford). 23(22):3191-3197, 1974.

Rat liver microsomes were shown to hydroxylate D- and L-amphetamine at the para position of the benzene ring. The identity of the product, p-hydroxyamphetamine, was established by the use of three different methods, paper chromatography, radio gas-chromatography and mass spectral analysis. The hydroxylation reaction was found to be linear with time to 15 min and protein concentration to 2mg/ml. The reaction followed Michaelis-Menten kinetics only at low substrate concentrations. When the concentration of D-amphetamine exceeded 0.5M the plot indicated substrate inhibition. 28 references. (Author abstract modified)

205437 Vogel, W.; Broverman, D. M.; Klaiber, E. L.; Kobayashi, Y. Worcester, MA **The relationship between the EEG driving response to light and plasma monoamine oxidase (MAO) levels.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):693-694, 1974.

A paper presented at the 8th International Congress of Electroencephalography and Clinical Neurophysiology reported a test of the hypothesis that monoamine oxidase (MAO) activity would be related to the degree of electroencephalogram driving in response to photic stimulation; i.e.,high MAO activity levels would be associated with high EEG driving. Subjects were ten normal males. For a 6-week period, peripheral blood was drawn daily from each subject. Plasma MAO activity was assayed. EEGs were taken daily, five times a week, for the six weeks. For an eleven-day period during the six weeks each subject was daily given 10mg of isocarboxazid, an MAO inhibitor; on the remaining days the subjects received a placebo. Double-blind procedure was used. For each subject the average MAO activity value over the 6-week period was computed; also, the average number of EEG driving responses. The correlation between MAO activity and EEG driving was 0.78, which supports the hypothesis that MAO activity level is directly associated with EEG driving in response to photic stimulation. (Author abstract modified)

205455 Stevens, Janice R.; Wilson, Karen; Foote, W.; Sawler, B. Boston, MA **EEG and schizophrenia: experimental studies, spectral analysis and "septal" spikes.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):702, 1973.

A paper presented at the 8th International Congress of the Electroencephalography and Clinical Neurophysiology, the physiologic and behavioral consequences of increasing the effect of dopamine on interneurons of an area strategically placed at the outflow of limbic structures subserving primary drive and memory functions. Dopamine activity was enhanced specifically in the mesolimbic pathway by local instillation of micro amounts of the gamma-aminobutyric acid (GABA) inhibitor, bicuculline, in the ventral tegmental nucleus of cats with chronically-implanted cannulas and electrodes, in order to block a putative GABA-coded negative feedback synapse on cells of origin for the mesolimbic dopamine pathway. A state of fear, catatonia and apparent hallucinosis follows, associated with remote random spike activity in nucleus accumbens septi, the superior terminus of the mesolimbic pathway. Similar results were not obtained by electrical or cholinergic stimulation of ventral tegmental nucleus, or by instillation of the GABA blocking agent in substantia nigra. These experimental data are considered in relation to results obtained from power spectral analysis of electroencephalogram (EEG) samples recorded during a stimulus response program designed for detection of subcortical spike activity in epileptic and schizophrenic man. (Author abstract modified)

205459 Ookawa, T. Gifu, Japan **Behavioural and electrographic observations during epileptic convulsions induced by strychnine and pentylenetetrazol in conscious young and adult chickens.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):707, 1973.

A paper presented at the 8th International of Electroencephalography and Clinical Neurophysiology reported behavioral and electroencephalographic (EEG) observations during epileptic convulsions induced by strychnine and pentylenetetrazol in conscious young and adult chickens. The strychnine spikes in the Wulst EEG were induced by intraperitoneal injection in young chicks, 1 to 14 days after hatching, and in adult hens. Large spontaneous bilaterally synchronous spikes are reliably produced by an intraperitoneal injection of strychnine as well as by pentylenetetrazol (Metrazol), whereas lower doses of strychnine elicited a spike-like wave of smaller amplitude. It was observed that large doses of strychnine produced a marked tonic convulsion and birds died within a few minutes after administration. Artificial respiration is important for the demonstration of large synchronous spikes in the EEG of birds. (Author abstract modified)

205467 Willey, T. J.; Hunt, G. M.; Peters, M. A. Loma Linda, CA **Computer analysis of methadone effects on the electroencephalogram.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):715, 1973.

A paper presented at the 8th International of Electroencephalography and Clinical Neurophysiology reported the acute effects of intravenous administration of methadone on spontaneous brain activity in the adult cat. Subtle frequency shifts or alterations attributed to methadone treatment were apparent. Multivariate statistical analyses were applied to the frequency spectra to ferret out significant features related to the drug-induced changes. The major effects were observed in the occipital and prepyriform cortex, with less effects observed in hippocampus, caudate nucleus and reticular formation. In general the pattern was consistent with behavioral alerting. (Author abstract modified)

205491 Celesia, G. G.; Booker, H. E.; Sato, S. Madison, WI **Effects of diazepam on experimentally induced cortical epilepsy and their correlation with drug concentration.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):727, 1973.

At the 8th International Congress of Electroencephalography and Clinical Neurophysiology, the effects of diazepam on experimentally-induced cortical epilepsy and their correlation with drug concentration were reported. Diazepam was administered intravenously to cats with penicillin-induced focal seizures. Diazepam transiently suppressed focal ictal activity and self-sustained afterdischarges. It was less effective in suppressing interictal spikes. It is suggested that diazepam acts mainly on cortical interneurons and polysynaptic systems. Brain and serum diazepam concentrations were determined by gas chromatography. Five minutes after administration of the drug, brain concentrations were greater than those of serum and remained higher throughout the period of observation (1 hr). The relationship between brain serum concentrations and the electrocorticographic changes will be discussed. (Author abstract modified)

205492 Rieger, H.; Krieglstein, J. no address **Effects of psycho-active tricyclic drugs on the EEG of the isolated perfused rat brain.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):730, 1973.

At the 8th International Congress of Electroencephalography and Clinical Neurophysiology, the effects of psychoactive tricyclic drugs on the electroencephalogram (EEG) of the isolated perfused rat brain were reported. The study was performed on 50 animals with the following drugs in the perfusate: promazine, imipramine, desipramine, and monodesmethylpromazine. The results describe the quantitative values and the visual EEG patterns as a function of the drug administered and the perfusion time. The differences and similarities between the EEG effects of different drugs are discussed and compared to the known psychopharmacological actions observed in patients. (Author abstract modified)

205507 Moyersoons, F.; Giurgea, C. Brussels, Belgium **Experimental EEG studies on barbiturate intoxication and piracetam.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):738, 1973.

At the 8th International Congress of Electroencephalography and Clinical Neurophysiology, experimental electroencephalogram (EEG) studies on barbiturate intoxication and piracetam were reported. Piracetam showed a protection in animals submitted to a lethal dose of barbiturates. In adult rabbits, EEG records were taken before, during and after barbiturate perfusion. A control animal, receiving the barbiturate alone, was always run at the same time as the treated animal. Piracetam given 1 h before secobarbital protected all 10 treated animals while out of the 10 controls only three survived. The treated animals showed fewer EEG silences when compared with the surviving controls. Piracetam given immediately after allobarbital protected 10 animals out of 13. As to EEG silences, the same phenomenon was observed as with secobarbital. (Author abstract modified)

205510 Spehlmann, R. Chicago, IL **The effects of acetylcholine and synaptic stimulation on the neurons in the sensorimotor cortex.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):741, 1973.

At the 8th International Congress of Electroencephalography and Clinical Neurophysiology, the effects of acetylcholine (ACh) and some of its antagonists, liberated from multibarreled micropipettes, on the spontaneous firing and the synaptic responses of single neurons in the pericruciate cortex of cats prepared as encephale isole were reported. ACh produced a slow and sustained increase of firing in many neurons and a fast and often unsustained increase of firing in some others. Atropine and scopolamine, while antagonizing the effect of extrinsic ACh, did not block the synaptic responses except in some of those neurons which reacted to ACh by excitation. In these neurons the muscarinic cholinolytics blocked the excitatory phases of the responses to reticular stimulation without affecting the responses to other stimuli. The selective block of one input is consistent with the view that, if ACh is a synaptic transmitter in the brain, it may be engaged in the transmission of reticular excitation to some cortical neurons. (Author abstract modified)

205546 Eskazan, E.; Akcasu, A.; Zembilci, N. Istanbul, Turkey **The effects of lithium carbonate on sleep and wakefulness in the cat.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):771, 1973.

At the 8th International Congress of Electroencephalography and Clinical Neurophysiology, a polygraphic search of the effects of lithium carbonate on sleep and wakefulness patterns of the cat was discussed. In all chronically normal cats with implanted macroelectrodes in cortex, lateral geniculate body, neck muscles and frontal sinuses (for electro-oculogram), the effects of lithium carbonate on the polygraphic patterns of wakefulness, slow wave sleep and paradoxical sleep (REM periods) is recorded. The blood level of lithium is determined concomitantly and the findings are compared with those obtained before the administration of lithium carbonate to the same cat. (Author abstract modified)

205578 Metys, J.; Metysova, J. Research Institute for Pharmacology, 17 Kourimska, 130 00 Praha 3, Czechoslovakia **Pharmacological properties of a potential tranquilising agent mesylphenacyrazine: I. Interaction with drugs influencing the nervous system.** Activitas Nervosa Superior (Praha). 16(3):161, 1974.

At the 16th Annual Psychopharmacological Meeting, a study of the interaction of mesylphenacyrazine with drugs influencing the nervous system in mice and rats was reported. Mesylphenacyrazine provided an effective protection against d,l-amphetamine-induced lethality in aggregated mice and rats at a dose range comparable to that inducing central depression in the observational and instrumental procedures. Even in high doses, mesylphenacyrazine did not reveal any central antidopaminergic action in several animal species. It exercised a certain inconsistent central anticholinergic action (vs. arecoline, oxotremorine) in mice. Mesylphenacyrazine showed further a mild antagonism against nicotine-induced tonic extensory convulsions in mice at higher doses. Caffeine convulsions and the caffeine toxicity in mice were reduced significantly by pretreatment with mesylphenacyrazine. 2 references.

205579 Wildt, S.; Metys, J.; Bartosova, M. Research Institute for Pharmacy, 533 51 Rosice nad Labem, okr. Pardubice, Czechoslovakia **Pharmacological properties of a potential tranquilising agent mesylphenacyrazine: II. Changes related to its repeated administration.** Activitas Nervosa Superior (Praha). 16(3):162, 1974.

At the 16th Annual Psychopharmacological Meeting, short-term experiments were reported demonstrating changes in toxicity and some pharmacological effects of mesylphenacyrazine in mice and rats (i.e.,inhibition of general motor activity registered in the Animex apparatus, prolongation of thiopental sleeping time, hypothermia, motor incoordination in the rotarod test). Under these circumstances the tolerance development to these actions of this new drug, a phenylpiperazine derivative, could be shown. The biphasic changes in the hypothermic action of mesylphenacyrazine in the experiments with a daily increment in drug dosage in mice support the hypothesis. 3 references.

205583 Dlabac, A.; Kazdova, E. Biochemical Research Institute 17, Kourimska, Praha 3, Czechoslovakia **Long-acting neuroleptics of perathiepine group: VUFB-9977 (oxyprothepine decanoate).** Activitas Nervosa Superior (Praha). 16(3):166-167, 1974.

At the 16th Annual Psychopharmacological Meeting, the effects of esters of 8-substituted 10-(hydroxyalkyl-piperazine)-10,11-dihydrodibenzo(b,f)thiepin with saturated fatty acids dissolved in sunflower oil, tested in dogs (apomorphine vomiting action) and rats (conditioned avoidance response, CAR) were reported. The esters of the perathiepine group were compared with fluphenazine enanthate or fluphenazine decanoate. In acute experiments, VUFB-9977 named oxyprothepine decanoate showed in dogs a sufficient antiemetic activity against apomorphine chloride. Its antiapomorphine action lasted longer than that of fluphenazine decanoate. In rats, the suppression of fixed CAR and the inhibition of stereotypic activities elicited by apomorphine do not enable a more distinct differentiation in the duration of action between individual perathiepine-derived esters. Both techniques proved a long-lasting effect of oxypro thiepine decanoate in acute administration. 3 references.

04 MECHANISM OF ACTION: BEHAVIORAL

198222 Stripling, Jeffrey S.; Alpern, Herbert P. Department of Psychology, University of Colorado, Boulder, CO 80302 **Nicotine and caffeine: disruption of the long-term store memory and proactive facilitation of learning in mice.** Psychopharmacologia (Berlin). 38(4):187-200, 1974.

The effects of nicotine and caffeine on the long-term store of memory in mice were determined for a wide range of dosages. Male F1 mice were given two trials in an appetitive maze 24 h apart. Both nicotine and caffeine produced a dose-dependent disruption of performance in the trials following the injection series. In contrast, nicotine produced facilitation of performance in animals given a series of injections in the absence of previous training, and caffeine produced a strong trend in this direction. It was concluded that these drugs produced a strong trend in this direction. It was concluded that these drugs produced disruption of the long-term store of memory for the initial training and proactive facilitation of maze learning. The existence of separate and opposing effects of these drugs on different aspects of learning and memory was discussed. 57 references. (Author abstract modified)

198225 Rolls, E. T.; Rolls, B. J.; Kelly, P. H.; Shaw, S. G.; Wood, R. J.; Dale, R. University of Oxford, Department of Experimental Psychology, South Parks Road, Oxford, England **The relative attenuation of self-stimulation, eating and drinking produced by dopamine-receptor blockade.** Psychopharmacologia (Berlin). 38(4):219-230, 1974.

The relative attentuation of self-stimulation, eating and drinking produced by dopamine-receptor blockade was examined. Spiroperidol, which blocks dopamine (DA) receptors,

attenuated self-stimulation of the nucleus accumbens, septal area, hippocampus, anterior hypothalamus and ventral tegmental area. Dopamine is thus involved in self-stimulation of many sites (in addition to the lateral hypothalamus). Feeding was partly attenuated, and drinking was much less attenuated by the spiroperidol. Since the rats bar pressed for brain stimulation reward, chewed pellets to eat, and licked a tube to drink, dopamine-receptor blockade may attenuate complex motor responses most. Alternatively, the blockade could affect brain stimulation reward more than the controls of eating, and these latter more than the controls of drinking. Feeding and drinking were equally and severely attenuated when rats had to bar press to obtain food or water. Results suggest that dopamine-receptor blockade impairs eating, drinking and self-stimulation by interfering with complex motor responses. 20 references. (Author abstract modified)

198226 Ziskind, David; Amit, Zalman; Baum, Morrie Department of Psychology, Sir George Williams University, 1455 de Maisonneuve Blvd. West, Montreal 107, Quebec, Canada **Resistance to extinction of an avoidance response in rats following the administration of chlordiazepoxide (Librium) and diazepam (Valium).** Psychopharmacologia (Berlin). 38(3):231-238, 1974.

In a one-way avoidance task with rats, injections of Librium (chlordiazepoxide) following avoidance acquisition resulted in prolonged resistance to extinction of the avoidance response. This effect occurred regardless of whether the rats had had prior experience with Librium or whether they were naive with respect to the drug. The same results were found with the same task when low doses of Valium were used. However, at a higher dosage an extreme reaction of either no responding or a high number of responses to extinction occurred in the naive animals. The Librium and Valium effects were compared to similar effects obtained using ethanol and hashish resin. 19 references. (Author abstract modified)

198227 Singh, H. K.; Ott, T.; Matthies, H. Institute fur Pharmakologie und Toxikologie, DDR-301 Magdeburg, Leipziger Strasse 44, Germany **Effect of intrahippocampal injection of atropine on different phases of a learning experiment.** Psychopharmacologia (Berlin). 38(3):247-258, 1974.

The possible participation of the cholinergic synapses of the hippocampus in the regulation of the learning process was investigated by observing the effect of an intrahippocampal injection of the muscarinolytic atropine on acquisition, consolidation, and extinction in rats. The pretraining application of atropine impairs the learning ability significantly, but produces a considerable improvement of retention as compared to the controls. The postraining application of the same dose also produces a considerable improvement of retention. When atropine is given 1 min before the first extinction test, no significant effect is observed. It is assumed that atropine has two distinct effects: 1) it impairs acquisition, i.e.,has an aversive effect on short-term memory-related processes; 2) it has a positive effect on consolidation. It is concluded that atropine has different effects on the various phases of learning. 49 references. (Author abstract modified)

198228 Izquierdo, Ivan. Departmento de Fisiologia, Farmacologia e Biofisica, Instituto de Biociencas, UFRGS, Caixa Postal No. 592, 90.000 Porto Alegre, Brazil **Effect on pseudoconditioning of drugs with known central nervous activity.** Psychopharmacologia (Berlin). 38(3):259-266, 1974.

The effects on pseudoconditioning of drugs with known central nervous activity were examined. Rats were placed in a conventional shuttle box and submitted to buzzers and shocks presented in random sequence and with no temporal association. These rats made pseudoconditioned barrier crossing responses to the buzzer. The performance of these responses was enhanced by metrazol and trimethadione, depressed by amobarbital, phenobarbital, meprobamate, diazepam, chlorpromazine and reserpine, and unaffected by diphenylhydantoin, cannabidiol, caffeine, strychnine, picrotoxin and dibenamine. The enhancing effect of trimethadione, but not that of metrazol, was antagonized by dibenamine. The results support the notion that pseudoconditioning is a distinct behavioral entity with pharmacologic characteristics clearly different from those of avoidance conditioning. 32 references. (Author abstract modified)

198457 Anson, John E.; Chandler, B. J. Dept. of Psychology, Stephen F. Austin State University, Nacogdoches, TX 75961 **Chlorpromazine effects on self-punitive behavior.** Journal of General Psychology. 91(Second half):307-308, 1974.

Findings of Martin et al. (1971) that rats injected with chlorpromazine late in escape training fail to exhibit self-punitive behavior during extinction testing were replicated to insure that results were not due to dependent learning. Subjects received chlorpromazine or saline early or late in escape training and the self-punitive effect was shown for all subjects injected with saline. Rats receiving chlorpromazine, either early or late in escape training, subsequently failed to exhibit sustained performance during punished extinction and performed similarly to chlorpromazine injected subjects tested in regular extinction. Performance of chlorpromazine subjects during punished extinction reflected the peak effectiveness of the drug. 3 references.

198480 Poshivalov, V. P. Kafedra farmakologii Pervogo Leningradskogo meditsinskogo instituta im. I. P. Pavlova, Leningrad **/The influence of analgesics and neuroleptics on affective manifestations of pain./** Vliyaniye anal0getikov i neyroleptikov na affektivnyye proyavleniya boli. Farmakologiya i Toksikologiya (Moskva). 36(6):651-653, 1973.

The influence of potent analgesics and neuroleptics on affective components of pain-induced emotional reactions was studied in albino mice. Calibrated clamps weighing 500, 800, and 1400 grams were placed at the base of the tail for 15 second periods, while a metal rod was simultaneously placed in front of the mouse. Behavioral response was measured by the following scale: 0 -- absence of visible reaction; 1 -- quivering, jumping, turning; 2 -- turning towards object causing pain; 3 -- single bite at clamp; 4 -- battling with clamp; 5 -- intensive running, fighting and shrieking. Mice were tested when under the influence of fentanyl, morphine, droperidol and chlorpromazine. Selective inhibition by analgesics and neuroleptics of affective manifestations of pain, including the most highly integrated components of behavior, was noted. The effect of analgesics on the affective behavioral components of an emotional reaction to pain stimuli was found to be similar to that produced by neuroleptics. 9 references. (Journal abstract modified)

198482 Vikhlyayev, Yu. I.; Klygul0, T. A. Laboratoriya psikhofarmakologii Instituta farmakologii AMN SSSR, Moscow **/The influence of benzodiazepine series tranquilizers on various forms of operant animal behavior./** Vliyaniye trankvilizatorov benzdiazepinovogo ryada na razlichnyye formy operantnogo povedeniya zhivotnykh. Farmakologiya i Toksikologiya (Moskva). 36(6):657-663, 1973.

The influence of diazepam, nitrazepam and chlordiazepoxide was studied on five types of operant animal behavior as

manifested in rats. When the rats were given positive reinforcement, diazepam and nitrazepam, while failing to change simple operant behavior, affected complex forms of reflexes to a time and light signal. This caused an increase in the number of reactions and a redistribution in time of the number of reinforced and nonreinforced reactions. When progressing from a simple operant reflex to a more complex one, the tranquilizers initially made the process of stabilization more difficult. The tranquilizers eliminated the conflicting situation in rats' operant behavior brought about by the substitution of quinine for water. It is concluded that changes in operant behavior occurring under the influence of benzodiazepine series tranquilizers are connected with depression of the synaptic transmission in the inhibitory pathways on the level of the limbic system. 30 references. (Journal abstract modified)

198483 Allikmets, L. Kh. Kafedra farmakologii Tartuskogo Universiteta, Tartu, USSR /**The influence of antidepressants and neuroleptics on behavioral reactions elicited by lesion and excitation of the hippocampus.**/ Vliyaniye antidepressantov i neyroleptikov na povedencheskiye reaktsii, vyzvannyye razrusheniyem i razdrazheniyem gippokampa. Farmakologiya i Toksikologiya (Moskva). 36(6):664-667, 1973.

Changes in the orientation response, motor activities and aggressive-defensive reflexes elicited by destruction and stimulation of the hippocampus under the influence of antidepressants and neuroleptics were studied in cats and rats. Albino rats were subjected to bilateral electrolytic destruction of the hippocampus. Antidepressants and neuroleptics were injected intraperitonneally 60 minutes before conducting the experiments. Orientation response was measured by number of risings per minute. Motor activity was determined by an actometer which measured pulse variations. Aggressive-defensive reflexes were measured in volts by the threshold of elicited squeaks. The inhibitory effect of antidepressants on behavioral reactions was found to be weaker, and that of neuroleptics, stronger, as compared with effects in control rats. Cats were subjected to electrostimulation of the hippocampus and steel electrodes were attached to their brains. Parameters of stimulation remained constant. Antidepressants were found to exert a stimulating influence on behavioral responses in cats. 12 references. (Journal abstract modified)

198610 Nakahama, Hiroshi; Yamamoto, Mitsuaki; Sakurada, Shinobu; Shima, Keisetsu. Division of Neurophysiology, Institute of Brain Diseases, Tohoku University School of Medicine, Nagamachi, Sendai, Japan **Effects of cytidine diphosphate choline on the nervous system in cats.** Experimental Neurology. 45(2):220-227, 1974.

The effect of cytidine diphosphate choline (CDP-choline) on the nervous system was investigated in cats administered the compound in the lateral ventricle and intrathecal space and superficially on the cerebral cortex and peripheral nerve. Almost immediately after intraventricular of 0.2mg/kg, administration subjects exhibited EEG and behavior arousal; 0.8mg/kg resulted in continuous crying and 10mg/kg in intense continuous crying and pronounced tachypnea. Effects lasted for 1-2 hr. Immediately after lumbar intrathecal administration of not less than 2.0-4.0mg/kg, EEG and behavior arousal occurred and lasted over 8 min. Administration of 10-20mg/kg caused hyperreflexia, and subjects bit the caudal region of the body. Applied superficially on the cerebral somatic sensory area I, CDP-choline potentiated and postsynaptic component of the potential evoked by ventrobasal thalamic stimulation; presynaptic component remained unchanged. Direct application to nerve fibers produced spontaneous impulse activity. Results suggest that CDP-choline exhibits marked excitatory effects on the nervous system, and that it acts directly upon synapses as well as on nerve fibers. 8 references. (Author abstract modified)

198612 Wise, Roy A.; Chinerman, J. Center for Research in Drug Dependence, Dept. of Psychology, Sir George Williams Univ., Montreal 107, Quebec, Canada **Effects of diazepam and phenobarbital on electrically-induced amygdaloid seizures and seizure development.** Experimental Neurology. 45(2):355-363, 1974.

Development of seizures in response to repeated amygdaloid electrical stimulation (kindling) was assessed after administration of diazepam, phenobarbital and diphenylhydantoin in rats. Daily 1 sec trains of biphasic square wave pulses elicited after discharge under all conditions and produced full motor seizures in a median of 9 days in control and 9 days in diphenylhydantoin. Afterdischarge, but not seizures, occurred after 14 days of stimulation in diazepam and phenobarbital conditions. When diazepam and phenobarbital subjects were subsequently stimulated to full seizure in the nondrugged condition, no savings occurred. Afterdischarge thresholds were unaffected by diazepam but were doubled by phenobarbital. Motor seizure could not be evoked by diazepam or phenobarbital, and neither interferred with the decrease in local afterdischarge threshold which was produced by repeated stimulation. Both drugs attenuated propagation of afterdischarge to the contralateral amygdala. The ineffectiveness of diphenylhydantoin may have been due to inadequate dosage or may have reflected the relative ineffectiveness of this drug with clonic seizures. 19 references. (Author abstract modified)

198733 Gomita, Yutaka; Ogawa, Nobuya. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu University Maedashi 3-1-1, Higashi-ku, Fukuoka City, Japan **Dissociation of general behavior produced by psychotropic drugs in mice.** Journal of Japanese Psychosomatic Society (Tokyo). 14(3):176-185, 1974.

The effects of d-methamphetamine (DM) or chlorpromazine (Cp) on dissociation of general behavior in mice in an open field situation were studied. In mice treated with saline solution, ambulation gradually decreased due to habituation. In mice treated with DM, ambulation markedly increased; and it returned to the level observed in the control mice after termination of DM treatment. In mice treated with DM and saline solution on alternate days, high scores of ambulation under DM influences and low scores under saline treatment were observed. The changes in rearing showed the same tendency. In mice treated with Cp daily, ambulation markedly decreased and returned to the level of the control mice after termination of Cp treatment. In mice treated with Cp and saline solution on alternate days, ambulation under saline treatment showed a higher score than that of the control mice. DM and Cp caused dissociation in learning tasks and in general behavior in an open field situation. 18 references. (Author abstract modified)

198897 Slonim, Philip S. Lehigh University **The effect of differential saline and cycloheximide states on the acquisition of a spatial reversal task in mice and rats. (Ph.D. dissertation)** Dissertation Abstracts International. Ann Arbor, Mich., Univ. Mfilms, No. 74-6702, HC$12.50 MF$4.00 77 p.

The nature of cycloheximide-induced amnesia was studied in mice and rats using a spatial discrimination reversal procedure. Subjects were trained in the spatial discrimination task (10 trials) on day one, 30 minutes after a subcutaneous injection of saline or cycloheximide. Recall of day-one training was as-

sessed by requiring the subject to reverse the assigned day one contingency on day two. Retention of day one training was measured by number of day two errors and first trial correct responses on day two. Overall results indicate that, at least with a relatively simple task, cycloheximide-induced amnesia in rats and mice is more consistent with a state-dependent than the consolidation model. This holds that such amnesia is not caused by the protein-synthesis-inhibiting effect of the drug, but by state-dependent deficits brought about by differential acquisition and retest states. (Journal abstract modified)

199039 Moss, Donald Eugene. Colorado State University **Puromycin and memory. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-5437 HC$12.50 MF$4.00 59 p.

The effect of intracranial injections of atropine on the amnesic effect of intracranial injection of puromycin, an inhibitor of protein synthesis which interferes with recall of memory, was examined in rats. Subjects were taught a position discrimination habit and 2 weeks later a reversal of the original habit, followed by intracranial injections. Retention was measured by a relearning of the reversal habit. Puromycin caused amnesia if multiple injections were made into the area of the ventral hippocampus and entorhinal cortex. Atropine was effective in reducing the effect. Findings provide in vivo support for the hypothesis that puromycin interferes with the recall of memory by affecting cholinergic neurotransmission. Atropine did not, however, eliminate the puromycin-induced amnesia. It is possible that interference with cholinergic neurotransmission is only one of several mechanisms by which puromycin blocks the recall of recent memories. (Journal abstract modified)

199211 Fanelli, Ottorino. Department of Pharmacology, Istituto Gentili, Via Mazzini, 112, 56 100 Pisa, Italy **Pharmacological and toxicological study of a new psychotropic stimulant: the 2-phenyl-5-dimethyl-tetrahydro-1,4-oxazine, in comparison with d,l-amphetamine, phenmetrazine and pemoline-Mg.** Arzneimittel-Forschung (Aulendorf). 23(6):810-816, 1973.

The CNS stimulating properties of 2-phenyl-5-dimethyl-tetrahydro-1,4-oxazine (G 130) was studied in laboratory animals and compared with phenmetrazine, d,l-amphetamine and pemoline-Mg. G 130 possesses an anorectic activity similar to phenmetrazine, with which it has an analogous structure. Furthermore G 130 has a motor-stimulating action, an antifatigue action and it enhances learning and memory of conditioned avoidance responses. All these properties are more interesting than those of d,l-amphetamine and pemoline-Mg. After repeated treatments, the stimulating properties of G 130 do not lead to tolerance, as occurs instead with d,l-amphetamine. For this reason and because of its relatively low toxicity, G 130 has an interesting pharmacological outline. 12 references. (Author abstract)

199213 Heinemann, H.; Stock, G. I. Psychologisches Institut der Universitat Heidelberg, Akademiestr. 3, Germany **Chlordiazepoxide and its effect on sleep-wakefulness behavior in unrestrained cats.** Arzneimittel-Forschung (Aulendorf). 23(6):823-825, 1973.

In unrestrained cats the alteration of sleep wakefulness patterns caused by infusion of 0.18mg/kg 7-chloro-2-methylamino-5-phenyl-3H-1,4-benzodiazepine-4-oxide (chlordiazepoxide, Librium) was tested. In order to diagnose the different sleep-wakefulness phases, the EEG (electroencephalogram), EOG (electrooculogram), EMG (electromyogram), and blood pressure were recorded continuously for 10 hours. Chlordiazepoxide has a sleep-inducing effect comparable to that of the benzodiazepine derivative medazepam. It increases the total sleeping time (synchronized and desynchronized sleep) by 1.6hours. The number of single phases of wakefulness is lowered by chlordiazepoxide infusion; the number of synchronized and desynchronized sleep phases, respectively, is increased. The duration of single phases is not significantly changed by chlordiazepoxide application. The mechanisms by which benzodiazepines may interfere with the sleep-wakefulness regulation are discussed. 16 references. (Author abstract)

199381 Foulon, C. Avenue de la Foret, 10, B-1050 Bruxelles, Belgium /**The effect of cycloheximide and actinomycin D on the spontaneous and operative behaviors of the pigeon. Preliminary note.**/ Action de la cycloheximide et de l'actinomycine D sur les comportements spontanes et operants du pigeon. Note preliminaire. Acta Neurologica Belgica (Bruxelles). 74(3):147-154, 1974.

The effect of cycloheximide and actinomycin-D on the spontaneous and operative behaviors of three groups of pigeons were studied: controls, pigeons treated with cycloheximide and pigeons treated with actinomycin-D. It was noticed that in the first group, spontaneous activity increased during different trials and that learning was rapid. In the second group, spontaneous activity remained constant during successive experiments while learning improved slowly. In the third group, spontaneous activity gradually disappeared and learning was nonexistent. There is a parallelism between spontaneous and operative behavior in the control groups as well as in the treated animals. 18 references. (Journal abstract modified)

199425 Vuillaume, Monique; Berkaloff, Andre. Laboratoire de Zoologie (ERA 227), Universite de Paris Sud, 91405 Orsay, France **LSD treatment of Pieris brassicae and consequences on the progeny.** Nature (London). 251(5473):314-315, 1974.

In studies of LSD treatment of Pieris brassicae, abnormalities in the behavior of the progeny were observed. Three generations were followed. It is suggested that the most probable target for LSD is the genetic material present in the germinal cells of the parental generation. 6 references.

199461 Balthazart, Jacques. Laboratoire de Biochimie generale et comparee, Universite de Liege, 17 Place Delcour, 4000 Liege, Belgium **Short-term effects of testosterone propionate on the behaviour of young intact male domestic ducks (Anas platyrhynchos).** Psychologica Belgica (Louvain). 14(1):1-10, 1974.

The short-term behavioral effects of massive injections of testosterone propionate (TP) in the domestic duck are examined. Five of the six major social displays and rapes of the females occur significantly more often in injected than in noninjected birds. The occurrence of these behaviors is, however, not associated with the increase in aggression reported by different authors. Penis growth is shown to be stimulated by the TP injections. Possible explanations are suggested to account for the low aggressivity of the injected males and the nonoccurrence of one social display (down-up) while five others do occur. 21 references. (Author abstract modified)

199550 Egger, Garry J.; Livesey, Peter J.; Dawson, Ronald G. Dept. of Psychology, University of Western Australia, Nedlands, Western Australia 6009, Australia **Ontogenetic aspects of central cholinergic involvement in spontaneous alternation behavior.** Developmental Psychobiology. 6(4):289-299, 1973.

The development of spontaneous alternation behavior in rats was studied in four experiments and this behavior was found to increase from a rate of around 20% in 15- to 16-day-old rats to around 90% in 100-day-old rats. Increasing the length of confinement in the first chosen goal arm did not affect alternation rates. Spontaneous alternation could be disrupted or facilitated in mature animals by the administration of either scopolamine hydrobromide or physostigmine sulphate; these drugs had no effect on the typical alternation pattern of 16-day-old rats but appeared to begin to have an effect at around 24 days. Dose response curves revealed certain age/dose level interactions which were consistent with the hypothesis that cholinergic inhibitory mechanisms in the brain develop gradually in the rat. 21 references. (Author abstract modified)

199864 Cools, Alexander R.; Janssen, Hendrik-Jan. Department of Pharmacology, University of Nijmegen, Nijmegen, The Netherlands **The nucleus linearis intermedius raphe and behaviour evoked by direct and indirect stimulation of dopamine-sensitive sites within the caudate nucleus of cats.** European Journal of Pharmacology (Amsterdam). 28(2):266-275, 1974.

The behavioral effects in cats elicited by unilateral, reversible lesions in the nucleus linearis intermedius raphe which modulate behavioral effects elicited by local application of dopamine into the caput nuclei caudati rostromedialis or by systemic injections of apomorphine were studied. The data suggest that the nucleus linearis is an indispensable link in the chain of intracaudate events triggered by direct or indirect activation of dopamine sensitive sites within the caudate nucleus and strengthen the hypothesis that there exists a transsynaptic relationship between nigro-caudate, dopaminergic and raphe-caudate, serotonergic fibres. The implication of the data is discussed with reference to the usefulness of a number of presently accepted test models in psychopharmacological research. 37 references. (Author abstract)

199866 Sanger, David J.; Steinberg, Hannah. Department of Pharmacology, University College London, London WC1E 6BT, England **Inhibition of scopolamine-induced stimulation of Y-maze activity by alpha-methyl-p-tyrosine and by lithium.** European Journal of Pharmacology (Amsterdam). 28(2):344-349, 1974.

The inhibition of scopolamine-induced stimulation of Y-maze activity by alpha-methyl-p-tyrosine and by lithium was reported. A singe dose of scopolamine markedly increased the spontaneous activity of rats when tested in a Y-shaped runway as compared with saline controls. When the animals were retested in the maze 24 hr later, this time without any drugs having been administered, those which had previously been tested under the influence of the drug were again more active than the saline controls. Pretreatment before the first trial with either alpha-methyl-p-tyrosine or lithium chloride blocked the immediate stimulant action of scopolamine though it did not significantly modify the after-effect. 29 references. (Author abstract)

199910 Otsuka, Masaru; Tsuchiya, Toshiro; Kitagawa, Sumio. Takarazuka Research Laboratories, Sumitomo Chemical Co., Ltd., Hyogo, Japan **Electroencephalographic and behavioral studies on the central action of nimetazepam (S-1530) in cats.** Arzneimittel-Forschung (Aulendorf). 23(5):645-653, 1974.

Electroencephalographic and behavioral analysis on the central action of 1-methyl-7-nitro-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one (nimetazepam, S-1530) in the cat was performed. Nimetazepam induced ataxia, grooming, suppression of aggressiveness and facilitation of appetite. The aggressiveness-reducing activity was more potent than that of diazepam. Changes induced by nimetazepam and nitrazepam in spontaneous electroencephalogram (EEG) were dissociation of the depth (limbic system and hypothalamus) EEG from the neocortical EEG. Nimetazepam and nitrazepam increased the waking state at the expense of sleep stages, especially of fast wave sleep, and delayed the onset of fast wave sleep. Nimetazepam and nitrazepam markedly elevated the threshold for manifestations of the hippocampal theta waves induced by stimulation of the ventromedial hypothalamus and midbrain reticular formation. Effects of nimetazepam and nitrazepam on duration of amygdala after discharge were biphasic changes which consisted of initially inhibitory and thereafter facilitatory actions. 8 references. (Author abstract modified)

199911 Costall, B.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, Yorkshire, England **Neuroleptic and non-neuroleptic catalepsy.** Arzneimittel-Forschung (Aulendorf). 23(5):674-682, 1974.

The cataleptic states induced by the neuroleptics of the phenothiazine and butyrophenone groups, reserpine and oxypertine were studied. The cataleptic states were reduced or abolished by lesions of the caudate putamen or globus pallidus, and potentiated by combination with the cholinergic agents arecoline and RS86. The catalepsies induced by the nonneuroleptic agents, metoclopramide and bulbocapnine, were similarly modified by the lesions but could be distinguished from the neuroleptic catalepsy by the failure to synergise with the cholinergic agents. In contrast to the neuroleptic agents, the cataleptic behavior of the narcotic analgesics, with the exception of M-6007, was enhanced rather than reduced by caudate-putamen and globus pallidus lesions. The results indicate that catelepsy is not exclusive to the neuroleptic drugs and that a drug-induced catalepsy is more likely to be neuroleptic-induced if it is potentiated by cholinergic agents, but loxapine and clothiapine are exceptions to this rule. The abolition of a cataleptic effect by the striatal or pallidal lesions is some indication of a neuroleptic catalepsy, but is not exclusive to these agents. 12 references. (Author abstract modified)

199956 Overstreet, D. H.; Vasquez, Beatriz J.; Russell, R. W. School of Biological Sciences, Flinders University of South Australia, Bedford Park South Australia 5042, Australia **Reduced behavioural effects of intrahippocampally administered carbachol in rats with low cholinesterase activity.** Neuropharmacology (Oxford). 13(10/11):911-917, 1974.

The effects of bilateral hippocampal administration of carbachol on discrete trial single alternation performance was studied in two groups of rats. One group was examined both before and after chronic treatment with diisopropyl fluorophosphate (DFP), an irreversible anticholinesterase agent; the other, before and after treatment with its arachis oil vehicle. Initially, carbachol, a cholinomimetic, produced a dose dependent decrease in the number of reinforced responses in both groups. A similar dose dependence was found after chronic treatment with arachis oil. However, rats chronically treated with DFP were unaffected. These results suggest that the sensitivity of cholinergic receptors in the hippocampus may be reduced during chronic treatment with DFP. This reduced sensitivity may be one mechanism underlying the development of behavioral tolerance to DFP. 27 references. (Author abstract)

199957 Nicholson, A. N.; Wright, Catherine M. Royal Air Force Institute of Aviation Medicine, Farnborough,

Hampshire, England **Inhibitory and disinhibitory effects of nitrazepam, diazepam and flurazepam hydrochloride on delayed matching behaviour in monkeys (Macaca mulatta).** Neuropharmacology (Oxford). 13(10/11):919-926, 1974.

The effect of three benzodiazepines, nitrazepam, diazepam, and flurazepam on total response time and on the accuracy of response on a delayed matching task has been studied in monkeys (macaca mulatta). Increased total response time was observed after all three doses of diazepam and particularly nitrazepam, but after flurazepam increased total response time was limited to the highest dose. Accuracy of response on delayed matching was impaired by all three drugs. The effect of diazepam and flurazepam was limited to the highest dose in each case, but with nitrazepam performance was impaired also after 0.45mg/kg. The effect of the three benzodiazepines on delayed matching was related in a complex way to the delay between stimuli and to the response demanded. It is suggested that the effect of the benzodiazepines depended on a complex interaction between the differential response of two systems leading to inhibited or disinhibited behavior. 8 references. (Author abstract)

199958 Tarsy, D.; Baldessarini, R. J. Department of Neurology, Boston University School of Medicine, Boston, MA **Behavioural supersensitivity to apomorphine following chronic treatment with drugs which interfere with the synaptic function of catecholamines.** Neuropharmacology (Oxford). 13(10/11):927-940, 1974.

Stereotyped gnawing behavior in the rat induced by apomorphine was studied from 1-4 weeks after withdrawal of drugs given daily for 3 weeks. Significant shifts in the dose response relationship toward increased sensitivity to the agonist were observed following alpha-methyl-p-tyrosine (MPT), reserpine, chlorpromazine or haloperidol, while promethazine, phenobarbital and diazepam were ineffective. It was not significant after only 11 days of chronic pretreatment with chlorpromazine, reserpine or MPT. The effective drug treatments did not lead to changes in spontaneous locomotor activity at the time of testing stereotyped responses. The appearance of increased behavioral sensitivity to apomorphine, a putative direct agonist of dopamine receptors in the corpus striatum and limbic system, when nonspecific withdrawal effects and changes in the metabolism of catecholamines or of the agonist were unlikely, suggest that the phenomenon of receptor supersensitivity following pharmacologically induced denervation may be involved. 54 references. (Author abstract modified)

199959 Davies, J. A.; Redfern, P. H. Department of Pharmacology, Welsh National School of Medicine, Heath Park, Cardiff CF4 4XN, Wales **The interaction of dopamine-antagonists and amantadine hydrochloride on the acquisition of the conditioned avoidance response in rats.** Neuropharmacology (Oxford). 13(10/11):941-948, 1974.

The interaction of amantadine hydrochloride (HCl) and dopamine antagonists on the acquisition of the conditioned avoidance response (CAR) has been studied. Pretrial injection of haloperidol or pimozide inhibited the acquisition of the CAR in a dose dependent manner. Amantadine HCl given 2 hr after haloperidol or pimozide reversed the inhibitory effects of these drugs on acquisition. The significance of these results is discussed in terms of the role of brain dopamine in learning and memory mechanisms. 19 references. (Author abstract)

199960 Green, A. R.; Grahame-Smith, D. G. M.R.C. Unit, Radcliff Infirmary, Oxford OX2 6HE, England **The role of brain dopamine in the hyperactivity syndrome produced by increased 5-hydroxytryptamine synthesis in rats.** Neuropharmacology (Oxford). 13(10/11):949-959, 1974.

The role of brain dopamine in the hyperactivity syndrome produced by increased 5-hydroxytryptamine synthesis in rats was examined. The syndrome of hyperactivity produced in rats by the administration of tranylcypromine followed 30 min later by tryptophan was inhibited by alpha-methyl-p-tryosine (MPT), a tyrosine hydroxylase inhibitor. While brain tryptophan and 5-hydroxytryptamine (5-HT) concentrations rose to levels observed in rats not pretreated with MPT, noradrenaline and dopamine concentrations were depleted by 75%. The administration of L-DOPA 1 hr after the second dose of MPT almost restored the brain dopamine concentrations, did not restore brain noradrenaline concentrations but did cause return of the hyperactivity produced by tranylcypromine and tryptophan. The hyperactivity response seen after administration of tranylcypromine and 5-methoxy-N,N-dimethyltryptamine which probably acts as a 5-HT analogue stimulating postsynaptic 5-HT receptor sites was completely inhibited by MPT pretreatment. Results are interpreted as indicating that at some point between the postsynaptic 5-HT receptor sites initiating the production of the hyperactivity syndrome and the mechanisms responsible for the expression of the syndrome, lies a system of dopaminergic neurones. 17 references. (Author abstract)

199963 Schechter, Martin D. Department of Pharmacology, Eastern Virginia Medical School, Norfolk, VA 23507 **Effects of propranolol, d-amphetamine and caffeine on ethanol as a discriminative cue.** European Journal of Pharmacology (Amsterdam). 29(1):52-57, 1974.

The effects of propranolol, d-amphetamine and caffeine on ethanol as a discriminative cue were studied. Rats were trained to escape a shock in a three-compartment chamber contingent upon their ability to discriminate between two drug states, namely, 1.5mg/kg ethanol and 0.9% saline. This discriminate ability was found to be dose responsive and was tested after pretreatment with 1, 5, 10 and 20mg/kg propranolol, 4.0mg/kg d-amphetamine sulphate and 100mg/kg caffeine. The results of the pretreatment experiments showed that, of the three possible antagonists, only amphetamine significantly decreased the rat's ability to discriminate between ethanol and saline. 30 references. (Author abstract)

199968 Everitt, Barry J.; Fuxe, Kjell; Hokfelt, Tomas. Department of Anatomy, University of Cambridge, Downing St., Cambridge CB2 3DY, England **Inhibitory role of dopamine and 5-hydroxytryptamine in the sexual behaviour of female rats.** European Journal of Pharmacology (Amsterdam). 29(1):187-191, 1974.

Drugs which interfere with either dopamine (DA), serotonin (5-HT) or noradrenaline (NA) transmission in the central nervous system were given to estrogen- and estrogen-+-progesterone-treated female rats and observations were made on their sexual behavior. Decreasing either DA or 5-HT transmission enhanced the sexual receptivity of estrogen-treated females, while increasing-DA and/or 5-HT-decreasing NA inhibits this behavior to varying degrees in estrogen-+-progesterone treated females. The results suggest specific roles for these amines in controlling sexual receptivity. 19 references. (Author abstract)

200036 Davis, W. Marvin; Borgen, Lowell A. Department of Pharmacology, University of Mississippi School of Pharmacy, University, MS **Effects of cannabidiol and delta9-tetrahydrocannabinol on operant behavior.** Research Communications in Chemical Pathology and Pharmacology. 9(3):453-462, 1974.

The effects of cannabidiol (CBD), a relatively inactive constituent of cannabis, on behavioral actions of delta9-tetrahydrocannabinol (THC) were studied. CBD pretreatment in both rat and pigeon significantly reduced the depressant effects of THC on variable-interval and fixed-interval schedules of food-reinforced operant behavior. The doses of CBD employed had no effect on the behavioral parameters, although higher doses did produce behavioral inhibition. The data suggest that cannabidiol may function as a partial agonist in relation to certain effects of THC. 19 references (Author abstract)

200039 Colpaert, Francis C.; Lal, Harbans. Janssen Pharmaceutics Research Laboratories, B-2340 Beerse, Belgium **Potentiation of jumping behavior by aminophylline in mice treated with threshold doses of amphetamine and dopa.** Research Communications in Chemical Pathology and Pharmacology. 9(3):587-590, 1974.

Upward jumping in mice caused by the combined administration of amphetamine and L-DOPA given in large doses is reported. With only threshold doses of the above combination, intense jumping was obtained following pretreatment with aminophylline (10, 20, 40, 80, 160mg/kg). Pimozide, but not phentolamine, effectively inhibited this jumping behavior. 10 referemces. (Author abstract)

200042 Ahlenius, Sven. Department of Pharmacology, University of Goteborg, Fack, S-400 33 Goteborg 33, Sweden **Effects of low and high doses of L-dopa on the tetrabenazine or alpha-methyltyrosine-induced suppression of behaviour in a successive discrimination task.** Psychopharmacologia (Berlin). 39(3):199-212, 1974.

The effect of the administration of L-Dopa on the alpha-methyltyrosine methylester HCl (MT) or tetrabenazine (TBZ) induced suppression of a successive discrimination conditioned avoidance task was studied. It was found that administration of the high L-Dopa dose resulted in a reversal of the MT or TBZ-induced suppression of the avoidance behavior, although the discrimination was lost. Restoration of the avoidance behavior and the correct discrimination was obtained with the low L-Dopa dose after MT but not after TBZ. The difference in the behavioral response to L-Dopa after MT as compared to the response obtained after TBZ is discussed in terms of the availability of the catecholamines formed from L-Dopa for release by the nerve impulses. 33 references. (Author abstract modified)

200043 Sofia, R. Duane; Barry, Herbert, III. Department of Pharmacology and Toxicology, Wallace Laboratories, Half Acre Road, Cranbury, NJ 08512 **Acute and chronic effects of delta9-tetrahydrocannabinol on food intake by rats.** Psychopharmacologia (Berlin). 39(3):213-222, 1974.

The effects of intraperitoneally injected delta9-tetrahydrocannabinol (THC) were compared with d-amphetamine sulfate (d-AMP) on food intake in rats which were given access to food for 6 hrs each day. Food intake was markedly reduced in a dose related fashion by THC in the first 2 hrs after drug administration. This anorexic effect persisted for the next 4 hrs and even on the next day. The anorexic potency of d-AMP was approximately twice that of THC in the initial 2 hrs interval after a single dose, but during the next 4 hrs and on the next day there was a compensatory increase in food consumption. Daily administration of THC for 9 days greatly decreased food intake and body weight gain of animals which were injected immediately before feeding, but had little effect on animals injected 16 hrs before feeding. 25 references. (Author abstract)

200046 McKim, W. A. Department of Psychology, Memorial University of Newfoundland, St. John's, Newfoundland, Canada **The effects of scopolamine and physostigmine on fixed-interval behaviour in the rat.** Psychopharmacologia (Berlin). 39(3):237-244, 1974.

In order to determine if two drugs, scopolamine and physostigmine, which have opposite effects on cholinergic transmission also produce opposite effects on fixed-interval (FI) performance, scopolamine and a wide range of doses of physostigmine were administered singly and concurrently to a number of rats responding on a FI 2 min schedule. Scopolamine produced a disruption in FI curvature which could be antagonized by physostigmine, but physostigmine by itself produced no consistent change. 15 references. (Author abstract)

200047 Minck, K.; Danneberg, P.; Knappen, F. c/o Fa. E. Merck, D-6100 Darmstadt, Frankfurter Strasse 250, Bundesrepublik Germany /**Effects of psychotropic drugs on exploratory behavior of mice.**/ Wirkungen von Psychopharmaka auf das Explorationsverhalten von Mausen. Psychopharmacologia (Berlin). 39(3):245-257, 1974.

The effects of psychotropic drugs on exploratory behavior of mice were studied. The sedative properties of chlorpromazine, haloperidol, and reserpine were represented by a simultaneous decrease of exploration and locomotion. Chlordiazepoxide, oxazepam, and diazepam in low doses caused an increase of locomotion, in higher doses a decrease of exploration, and finally an inhibition of both types of behavior. After phenobarbital the locomotion and exploration of the animals was considerably increased. Amphetamine caused a significant inhibition of exploration in low doses which did not increase locomotion. When locomotion was enhanced the exploration still remained depressed. Imipramine in large doses caused a decrease of both locomotion and exploration. No equivalents could be found for the antidepressant properties of the drug. Mescaline caused an increase of locomotion and a decrease of exploration, but only in a dose range which has to be considered neurotoxic. 32 references. (Author abstract)

200054 Booth, D. A.; Nicholls, Joy. Department of Psychology, P. O. Box 363, Birmingham B15 2TT, England **Behavioral specificity of chloralose-induced feeding in the rat.** Psychopharmacologia (Berlin). 39(2):145-150, 1974.

Behavioral specificity of chloralose-induced feeding in the rat was studied. The latency of feeding in the satiated rat was markedly shortened after intraperitoneal injection of chloralose. Feeding generally began before the onset of drinking or sedation. The optimum dose to facilitate food intake appeared to be lower at night than by day. Chloralose has a primary appetite-inducing effect which is much more powerful than that of 2-deoxyglucose. 12 references. (Author abstract)

200055 Dykstra, Linda A.; McMillan, D. E.; Harris, L. S. Department of Psychology, University of North Carolina, Chapel Hill, NC 27514 **Antagonism of morphine by long-acting narcotic antagonists.** Psychopharmacologia (Berlin). 39(2):151-162, 1974.

The effects of three narcotic antagonists, diprenorphine, naltrexone, and naloxone were studied on the schedule controlled behavior of pigeons. Naltrexone decreased the rate of responding under the fixed-interval and fixed-ratio components of a multiple fixed-interval, fixed-ratio schedule. Naltrexone and diprenorphine were equipotent in blocking the rate-decreasing effects of morphine on schedule-controlled behavior when the antagonists were given immediately before

morphine, and both were more potent morphine antagonists than naloxone. Higher doses of all three antagonists were required to block the effects of morphine as the time between the administration of the antagonist and morphine increased. Naltrexone provided a slightly better antagonism of morphine than diprenorphine when morphine was given 2 or 6 h after the antagonist and both antagonists had a longer duration of antagonist action than naloxone. 25 references. (Author abstract)

200637 Sathananthan, G.; Shopsin, B.; Petersson, Birger. Neuropsychopharmacology Research Unit, New York Univ. School of Medicine, New York, NY 10016 **The effects of lithium carbonate on serum gastrin in psychiatric patients.** Acta Psychiatrica Scandinavica (Kobenhavn). 50(1):86-89, 1974.

The effects of lithium carbonate on serum gastrin was studied in four psychiatric patients with different psychiatric diagnoses. All the patients showed normal serum values during the first 3 weeks of the treatment period. Possible reasons for the relatively unelevated levels are discussed. The effects of catecholamines on gastrin release are also mentioned as a lead in the study of the relationships between lithium, amines, gastrin and carbohydrate metabolism. 23 references. (Author abstract modified)

200748 Fuchimoto, Hideaki. School of Medicine, Kyushu University, Fukuoka, Japan **Aggressive behaviors induced by chronic administration of theophylline, with particular reference to alterations in behaviors of immature rats.** Fukuoka ACTA Medica (Fukuoka). 65(6):407-415, 1974.

The effect of chronic administration of theophylline on the development of aggressive behavior in immature rats was studied. Immature rats of 30 days of age and mature rats of 100 days of age were used. The reflexive fighting test and the aggressiveness rating test were used for the measurement of aggressive behaviors, and the open field test was performed to measure emotionality objectively. It was found that chronic administration of theophylline-induced aggressive behavior in immature rats as well as mature rats and that untreated immature rats, unlike mature rats, did not learn to fight in the repeated fighting situations. The theophylline-induced changes in emotionality among immature rats were considered similar to those in mature rats. Results are discussed. 22 references. (Author abstract modified)

200998 Robinson, R. G.; McHugh, P. R.; Bloom, F. E. Laboratory of Neuropharmacology, Special Mental Health Research Division, IRP, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Chlorpromazine-induced hyperphagia in the rat. (Unpublished paper).** Washington, D.C., NIMH, 24 p.

Chlorpromazine-induced hyperphagia was investigated in the rat. During a 4 month period, 20 rats treated with subcutaneous chlorpromazine (CPZ), at any dose tested, gained less weight than saline-treated controls. However, increased feeding did occur on the first day of CPZ treatment if the animal was drug free for at least 2 days prior to treatment. The "first day" hyperphagia was a time-limited response that did not occur until 8 hours after CPZ injection and lasted only 1 day. During the period of hyperphagia, treated animals showed increased motivation to obtain food. Although sedation is a marked effect of CPZ and may be the reason for the delayed onset of hyperphagia, sedation with a different drug does not cause hyperphagia. It is suggested that accumulation of a metabolite of CPZ may interfere with the feeding response and cause the hyperphagia to disappear after the first day of treatment. 16 references. (Author abstract modified)

201125 Chute, Douglas Lawrence. University of Missouri - Columbia **The engram, lost and found. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-18501 HC$12.50 MF$4.00 62 p.

Previous data from a variety of amnesic agents were interpreted for the retrieval hypothesis of retrograde amnesia, and memory storage mechanisms responsible for the phenomenon were reevaluated. Sodium pentobarbital induced state-dependent learning in rats for a bar-press shock avoidance task. Limited overtraining and multiple-state training affected dissociation. State-same evoked response patterns from the visual cortex reflected learning, but state-different response patterns did not. Results are interpreted in terms of statistical configuration theory of memory, where blocking of the readout component seems responsible for state change produced performance decrements. (Journal abstract modified)

201153 O'Boyle, Michael. Florida State University **Conditioned suppression of mouse killing in rats following radiation or lithium chloride injections. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-18081 HC$12.50 MF$4.00 86 p.

The conditioned suppression of mouse killing in rats by means of radiation and lithium chloride was investigated. In experiment one, conditioned suppression of killing was produced following pairings of mouse presentations (CS) with 96 roentgens of ionizing radiation (US) at 0 (2 min) and 30 min US-CS interstimulus intervals. No suppression occurred at CS-US intervals of 30 min, 1 hr, and 2 hr; or at US-CS intervals of 1 and 2 hr. In experiment two, subjects received CS-US pairings of mice and radiation (CS-US interval 2 min). Although rats that had been familiarized with mice prior to conditioning were less likely to show a suppression of killing than subjects irradiated after their first kill, the result was not significant. In experiment three, injections of LiCl immediately following a kill suppressed mouse killing in subjects that had shown no suppression following irradiation treatments in experiment one. Results are compared with prior work dealing with conditioned taste aversion and discussed in relation to the predatory nature of the rats' killing response and the idea that there exist biological constraints on learning. (Journal abstract modified)

201293 Tomkiewicz, Michal; Steinberg, Hannah. Dept. of Pharmacology, University College London, Gower Street, London WC1E 6BT **Lithium treatment reduces morphine self-administration in addict rats.** Nature (London). 252(5480):227-229, 1974.

The effect of lithium on the amount of voluntary ingestion of morphine by addict rats was investigated. Substantial reductions of sucrose morphine self-administration were obtained in two different experiments during lithium treatment. Since lithium did not alter the amounts of either sucrose quinine or sucrose consumed, results suggest that the reductions in the amount of morphine ingested during lithium in the sucrose morphine experiment did not result merely from changes in the palatibility of the fluids. 17 references.

201319 Holtzman, Stephen G. Emory University, Department of Pharmacology, Atlanta, GA 30322 **Tolerance to the stimulant effects of morphine and pentazocine on avoidance responding in the rat.** Psychopharmacologia (Berlin). 39(1):23-37, 1974.

Dose-response curves were determined for the effects of morphine and pentazocine on continuous avoidance responding in the rat. Each dose of morphine was retested following 3

days of morphine administration. The pentazocine curve was redetermined after 3 days of treatment with either pentazocine or morphine. Upon initial testing, morphine and pentazocine both generated biphasic dose-response curves. Graded increases in response rate were produced by 0.3-3.0mg/kg of morphine and by 1.0-10mg/kg of pentazocine; behavior was disrupted by 10mg/kg of morphine and by 30mg/kg of pentazocine. The stimulant effects of the lower doses of morphine and pentazocine were markedly reduced by 3 days of drug treatment; the disruptive effect of the highest dose of each drug was similarly attenuated. These findings show that tolerance can develop to a stimulant component of action of morphine and pentazocine in the rat. 29 references. (Author abstract modified)

201321 Kuhn, D. M.; Appel, J. B.; Greenberg, I. University of South Carolina, Department of Psychology, Columbia, SC 29208 **An analysis of some discriminative properties of d-amphetamine.** Psychopharmacologia (Berlin). 39(1):57-66, 1974.

Male albino rats were trained and tested on a two-lever discrimination task based upon the presence or absence of d-amphetamine. This compound was found to produce strong discriminative cues. A dose-effect function was ascertained and 50% response was attained at 0.23mg/kg d-amphetamine. In order to determine the effective duration of d-amphetamine action, the interval between injection and testing was varied; it was found that the discriminative effects of the drug began to dissipate between 60 and 90 min after injection. An attempt was made to compare the discriminative cues of other drugs with those of d-amphetamine, and in all cases, the rats responded predominantly on the saline related lever. Only methamphetamine produced d-amphetamine-like responding. Alpha-methyl-para-tyrosine (AMPT), a compound which depletes brain catecholamines, was found to disrupt the d-amphetamine-saline discrimination. 27 references. (Author abstract modified)

201322 Dandiya, P. C.; Kulkarni, S. K. Department of Pharmacology, S.M.S. Medical College, Jaipur-302004, India **A comparative study of d- and l-amphetamine on the open field performance of rats.** Psychopharmacologia (Berlin). 39(1):67-70, 1974.

Behavioral effects in the open field test following the administration of d-amphetamine and l-amphetamine were compared in rats. A significant difference was found between the effects of the two isomers on horizontal activity; d-amphetamine alone caused horizontal stereotypy. In both cases dose-response relations were curvilinear. On the other hand, although both isomers produced vertical stereotypy, the dose-response relations were generally monotonic increasing with no significant differences between isomers. These differential effects on behavior have been explained on the basis of stereospecificity of adrenergic neurons for amphetamine. The results of the study are consistent with earlier hypotheses that the horizontal and vertical stereotyped behaviors of rats in the open field situation are functions of brain noradrenergic and dopaminergic systems, respectively. 12 references. (Author abstract)

201843 Damitz, Charles; Tritt, John; Anderson, David; Goldstein, Melvin L. Indiana Univ., 2300 S. Washington St., Kokomo, IN 46901 **The effect of varying the dosage of sodium pentobarbital on the bar-press rate of rats.** Bulletin of the Psychonomic Society. 4(5A):471-472, 1974.

The effect of varying the dosage of sodium pentobarbital on the bar-press rates of rats was examined. The dose-response curve for sodium pentobarbital was determined for rats performing a simple bar-press response for water reinforcement 20 min after being injected with dosages of sodium pentobarbital ranging from 1.3mg/kg to 5.2mg/kg of bodyweight. Sodium pentobarbital, in the low doses used in the study, consistently depressed bar-press responding. The bar-press rate varied directly with the dosage of the drug. The low dosages of the drug used in the study apparently have a depressant effect on the central nervous system. 3 references. (Author abstract modified)

201915 Azbek0yan, S. G.; Lapin, I. P. Laboratoriya psikhofarmakologii, Leningradskogo nauchno-issledovatel0skogo psikhonevrologicheskogo instituta, Leningrad **/The effect of serotoninergic and adrenergic preparations upon alcohol-induced excitation in mice./** Vliyaniye serotninergicheskikh i adrenergicheskikh preparatov na alkogol0noye vozbuzhdeniye u myshey. Farmakologiya i Toksikologiya (Moskva). 37(4):393-396, 1974.

The effect of serotonergic and adrenergic preparations on alcohol-induced excitation in mice was studied. Injection of 1.5to 2mg/g of ethanol produced intensified locomotion in 15 minutes. With injection of serotonergic agents, Ib-503, BC-105 and, deseryl 30 minutes before introduction of the alcohol; or of para-chlorophenylalanine 20 minutes to 4 hours before injection of alcohol, no intensification of locomotion was observable. The serotonin precurser 5-oxytryptophane potentiated the action of ethanol. L-methyltyrosine did not influence the stimulating effect of ethanol: dioxyphenylalanine in combination with Ro 4-4602 prevented the stimulation normally produced by ethanol. 11 references. (Journal abstract modified)

201919 Lapin, I. P.; Oksenkrug, G. F.; Osipova, S. V.; Uskova, N. V. Laboratoriya psikhofarmakologii, Leningradskogo nauchno-issledovatel0skogo psikhonevrologicheskogo instituta, Leningard **/Potentiation with tricyclic antidepressants of the inhibitory action of apomorphine on the attitudinal reflex in frogs./** Usileniye tritsiklicheskimi antidepressantami tormozyashchego vliyaniya apomorfina na refleks perevorachivaniya u lyagushki. Farmakologiya i Toksikologiya (Moskva). 37(4):407-410, 1974.

The effect of tricyclic antidepressants on the inhibitory action of apomorphine was studied in frogs. Apomorphine was found to inhibit the righting reflex. The tertiary (chlorimipramine, imipramine, amitriptyline) and secondary (desmethylimipramine, nortriptyline) tricyclic antidepressants potentiated the effect of apomorphine. Neuroleptics haloperidol and thioproperazine did not affect the action of apomorphine potentiated by imipramine. The possible participation of serotonergic processes in the blocking effect of apomorphine and its potentiation by tricyclic antidepressants are discussed. 13 references. (Journal abstract modified)

202122 Yamamoto, Kenichi; Kimura, Yasushi; Naito, Yukio; Kido, Ryonosuke. Division of Neuropharmacology, Shionogi Research Laboratory, Osaka, Japan **Studies of conflict-induced behavior in the cat: behavior analysis and effects of psychotropic drugs.** Advances in Neurological Sciences (Tokyo). 15(1):33-50, 1971.

The effects of psychotropic drugs on conflict-induced behavior in cats conditioned to bar-press for food were studied. Food was substituted with a jet of air and attempts by the cats to get food were reduced. Cats who most quickly extinguished responding under negative conditioning increased food obtaining trials after injection with chlordiazepoxide.

Chlorpromazine had no effect on this group, but increased bar-pressing in cats who extinguished slowly. Phenobarbital increased bar-pressing in cats who had completely extinguished bar-pressing. Metamphetamine increased bar-pressing even without a food stimulus in cats slow to extinguished response under negative conditioning. 34 references.

202201 Kosersky, Donald S.; Harris, R. Adron; Harris, Louis S. Department of Medicinal Chemistry and Pharmacology, Northeastern University, Boston, MA 02115 **Naloxone-precipitated jumping activity in mice following the acute administration of morphine.** European Journal of Pharmacology (Amsterdam). 26(1):122-124, 1974.

Jumping behavior in mice elicited by naloxone as early as 10 min after acute administration of morphine is reported. The jumping response was determined to be time-dependent and a function of both morphine and naloxone dosage. It is suggested that jumping behavior in mice may result either from a sensitization or unmasking action by morphine to a stimulatory effect of naloxone or from an unantagonized stimulatory action of morphine. 7 references. (Author abstract)

202202 Flood, James F.; Rosenzweig, Mark R.; Bennett, Edward L.; Orme, Ann E. Department of Psychology, University of California, Berkeley, CA **Comparison of the effects of anisomycin on memory across six strains of mice.** Behavioral Biology. 10(2):147-160, 1974.

The effects of anisomycin on retention for step-through passive-avoidance training were compared across six strains of mice including pigmented and albinos, inbred and outbred, and strains light and heavy in weight. Widely-differing conditions of training were required in order for 90-100% of the mice in each strain to learn one trial passive-avoidance. A single injection of anisomycin, given 15 min prior to training, was found to cause significant amnesia for passive-avoidance training in all strains of mice. It was also found that a small increase in shock intensity decreased the percent amnesia caused by a single pretraining injection of anisomycin. If at this higher shock intensity the pretraining injection was followed by a second injection of anisomycin, given 1.75 hr after training, a high percentage of the subjects was again found to have amnesia. Possible causes of strain differences in ability to acquire the passive-avoidance habit are discussed. The necessity of protein synthesis for memory formation is considered. 7 references. (Author abstract modified)

202598 Arushanyan, E. B.; Belozertsev, Yu. A. Kafedra farmakologii Chitinskogo meditsinskogo instituta, Chita, USSR **/The effect of inhibitors of catecholamine synthesis (alpha-methyltryrosine and disulfiram) on the background activity of sensorimotor cortex neurons and their responses to afferent caudate and reticular stimulation./** Vliyaniye ingibitorov sinteza katekholaminov (a-metiltirozina i disul0frama) na fonovuyu aktivnost0 neyronov sensomotornoy zony kory i ikh otvety na afferentnuyu, kaudatnuyu i retikulyarnuyu stimulyatsiyu. Bulleten0 eksperimental0noy biologii i meditsiny (Moskva). 78(9):56-60, 1974.

The background activity of individual neurons of the sensorimotor cortex and their responses to light flashes, sound stimuli, clicks, electrical stimuli, and to stimulation of the caudate nucleus and the reticular formation of the midbrain were recorded in nonanesthetized and curarized cats. Administration of alpha-methyltyrosine and disulfiram 6 hours before the experiment promoted intensification of the grouping of background rhythmic activity, an increase in the number of background active units, and an increase of afferent short latent responses. Phasic and tonic inhibition of neurons with a low frequency stimulation of the caudate nucleus was intensified by alpha-methyltyrosine, and decreased by disulfiram. No blocking effect of phenamine on the caudate inhibition was expressed after alpha-methyltyrosine action. Both substances diminished the facilitatory and inhibitory reticular effects, disulfiram more than alpha-methyltyrosine. 15 references. (Journal abstract)

202666 Stitzer, Maxine. Baltimore City Hospitals, 4940 Eastern Ave., Baltimore, MD 21224 **Comparison of morphine and chlorpromazine effects on moderately and severely-suppressed punished responding in the pigeon.** Journal of Pharmacology and Experimental Therapeutics. 191(1):172-178, 1974.

In a study of the effects of morphine and chlorpromazine, keypeck responding of pigeons was maintained under a fixed-interval 3 minute schedule of food delivery. Simultaneously, electric shock was delivered under a fixed-ratio schedule for responses occurring during alternate schedule components. Shock intensity and frequency were adjusted to produce either moderate or severe response suppression in the punishment components. Chlorpromazine, under both levels of punishment severity, further decreased most rates of punished responding, while generally increasing comparable rates of unpunished responding. When punished responding was more severely suppressed, morphine further decreased very low rates of punished responding, but generally increased comparable rates of unpunished responding. The effects of both drugs on local rates within the intervals depended in an orderly way on control response rate. 19 references. (Author abstract modified)

202667 Downs, David A.; Woods, James H. Department of Pharmacology, University of Michigan Medical School, Ann Arbor, MI 48104 **Codeine- and cocaine-reinforced responding in rhesus monkeys: effects of dose on response rates under a fixed-ratio schedule.** Journal of Pharmacology and Experimental Therapeutics. 191(1):179-188, 1974.

Over a wide range of doses, codeine and cocaine both maintained lever press responding in rats when 30 responses were required for each intravenous injection. Rate of responding for each drug increased to a maximum and then decreased as dose (milligrams per kilogram per injection) increased. Maximum response rate for cocaine was over 3.5times greater than the maximum response rate for codeine. For both drugs, greatest stability of response rates across sessions was obtained at the higher doses, and changes in dose generally produced immediate changes in response rates. Injections of codeine were usually distributed in a negatively accelerated pattern within sessions while injections of cocaine were more evenly distributed. History of cocaine exposure appeared to increase response rates for low doses of cocaine in some monkeys. 16 references. (Author abstract modified)

202721 Syme, Lesley A.; Syme, G. J. Department of Psychology, University of Canterbury, Christchurch, New Zealand **The role of sex and novelty in determining the social response to lithium chloride.** Psychopharmacologia (Berlin). 40(1):91-99, 1974.

Effects of lithium chloride on the social behavior of male and female rats were measured in unfamiliar and familiar test situations using a photographic technique. Lithium treated females showed an increase in body contact and a decrease in social distances in comparison with saline treated controls in both test conditions. Males administered lithium showed increased corner occupancies in the novel test setting while in the familiar test they showed decreased body contact and in-

creased average group social distance in comparison with the saline condition. Further tests in an exploration box confirmed that lithium decreased the general environmental responsiveness of male rats. The results are discussed with reference to the antiaggressive effect of lithium. 27 references. (Author abstract)

202724 van Buskirk, Roderick; McGaugh, James L. Department of Psychobiology, University of California, School of Biological Sciences, Irvine, CA 92664 **Pentylenetetrazol-induced retrograde amnesia and brain seizures in mice.** Psychopharmacologia (Berlin). 40(1):77-90, 1974.

In three strains of mice (Ha/ICR, Swiss Webster and C57BL/6J), the influence of pentylenetetrazol injections on brain seizure activity recorded from cortical electrodes, and retrograde amnesia in an inhibitory avoidance task were examined. In Ha/ICR mice, pentylenetetrazol administered after training impaired retention in doses that elicited brain seizures as well as in doses just below those which elicit brain seizures. The degree of retention impairment decreased with increasing training-treatment intervals. In Swiss Webster and C57BL/6J mice, doses of pentylenetetrazol which produced brain seizures did not affect retention. The results indicate that elicitation of brain seizures is not a sufficient condition for producing retrograde amnesia with pentylenetetrazol. 20 references. (Author abstract)

202740 Charness, Michael E.; Amit, Zalman; Taylor, Max. Johns Hopkins School of Medicine, Baltimore, MD **Morphine induced stereotypic behavior in rats.** Behavioral Biology 13(1):71-80, 1975.

Morphine-induced stereotypic behavior in rats was studied. Five groups of male Wistar rats received five daily injections of three dose levels of morphine hydrochloride and one dose of d-l amphetamine. The occurrence of morphine-induced stereotyped behavior was measured and categorized into three subtypes. Diurnal influences on stereotyped behavior were also evaluated and an attempt was made to compare morphine and amphetamine stereotyped behavior. The effect of haloperidol on morphine and amphetamine stereotyped behavior was assessed. Since tolerance seemed to develop to the motor depressant effects of morphine, while no increases in stereotyped behavior were observed when it was measured as percentage of active time, it is suggested that tolerance does not develop with respect to stereotyped behavior. It is argued that morphine induced stereotyped behavior does not seem to be a rebound phenomenon dependent on the development of motor tolerance. 13 references. (Author abstract modified)

202758 Woodruff, Michael L.; Kearley, Richard C.; Isaacson Robert L. Department of Psychology, Middlebury College, Middlebury, VT 05753 **Deficient brightness discrimination acquisition produced by daily intracranial injections of penicillin in rats.** Behavioral Biology. 12(4):445-460, 1974.

Rats with unilateral epileptiform foci produced by daily injections of penicillin into either occipital cortex or hippocampus trained on an operant visual discrimination were examined. Both of the experimental groups were retarded in the acquisition of the discrimination, but the rats with foci in the occipital cortex demonstrated a more severe impairment, despite the fact that secondary epileptiform discharges appeared in hippocampus and visual cortex under both conditions. After 5-7 days of treatment this drug produced some slight seizure activity which was unrelated to performance. On Day 11 of discrimination training the rats receiving penicillin were injected with sodium sulfadiazine and the rats receiving sodium sulfadiazine were given penicillin. The rats changed from penicillin to sodium sulfadiazine showed an immediate increase in the percentage of correct responses. Rats switched from sodium sulfadiazine to penicillin demonstrated a transitory impairment in performance. The data indicated that epileptiform activity produced by penicillin results in a deficit in retrieval of recently formed memories. 19 references. (Author abstract modified)

202768 Miczek, Klaus A. Department of Psychology, Carnegie-Mellon University, Pittsburgh, PA 15213 **Intraspecies aggression in rats: effects of d-amphetamine and chlordiazepoxide.** Psychopharmacologia (Berlin). 39(4):275-301, 1974.

In a study of intraspecies aggression in rats, d-amphetamine sulfate and chlordiazepoxide hydrochloride, administered to either the dominant or subordinate rat, altered several components of fighting behavior in a dose-dependent biphasic manner. Low doses of amphetamine and chlordiazepoxide given i.m. to the dominant rat 30 min prior to 15 min tests increased attack bites and leaps and the display of aggressive postures and threats, whereas higher doses of both drugs suppressed attacks and threats. Amphetamine and chlordiazepoxide, administered to the subordinate rat, caused a more prolonged display of submissive supine and defensive upright postures; chlordiazepoxide prolonged immobile crouching whereas amphetamine greatly reduced this response. Drugged subordinate rats also provoked more attacks and threats by the nondrugged opponents. The multiresponse analysis of fighting reveals that various elements of aggressive and defensive submission behavior patterns are differentially sensitive to drug action. The results indicate that amphetamine and chlordiazepoxide can facilitate or inhibit attack or defense depending on the dose level and which of the opponents was injected, but do not reverse dominance-subordination relationships. 54 references. (Author abstract)

202769 Calhoun, William H.; Jones, Elisabeth A. Department of Psychology, University of Tennessee, Knoxville, TN 37916 **Methamphetamine's effect on repeated acquisitions with serial discrimination reversals.** Psychopharmacologia (Berlin). 39(4):303-308, 1974.

In rats trained through a series of discrimination reversals until they developed a stable, repeated acquisition baseline, methamphetamine accelerated acquisition measured from this baseline. The drug effect was demonstrated with successive cumulative records and with a graphic method using a distribution of error scores to develop a baseline. With low doses, methamphetamine reduced errors without affecting rewarded responding. This effect is dose-dependent, although at 1.0mg/kg the drug may disrupt operant behavior. 5 references. (Author abstract)

202770 Fontaine, O.; Libon, Ph.; Richelle, M. University of Liege, Psychologie Experimentale, 32, Bd. de la Constitution, Liege, Belgium **Action of a new psychotropic drug (Sulpiride) on avoidance behavior in rats.** Psychopharmacologia (Berlin). 39(4):309-314, 1974.

Sulpiride, a new psychotropic drug with neuroleptic activity, was administered to rats in a Sidman avoidance schedule. Doses ranging from 1-80mg/kg resulted in the animal receiving fewer shocks. This effect was not correlated with an increase of responding and seemed unrelated to the suppressing action abruptly observed at high doses. These results differ from those classically obtained with other neuroleptics. 7 references. (Author abstract)

202772 Nir, I.; Weller, C. P.; Sulman, F. G. Department of Applied Pharmacology, School of Pharmacy, Hebrew University, Jerusalem, Israel **Behavioural effect of intraventricular application of methoxy-indolealkylamines in the rat.** Psychopharmacologia (Berlin). 39(4):323-329, 1974.

Behavioral profiles of 23 biogenic tryptophan derivatives and related compounds were determined by injecting the substances into the lateral ventricles of unanaesthetized male rats using the Feldberg technique. The synthetic compound 5,6,7-trimethoxy-N-dimethyl-tryptamine (TNDT) was found to act quite differently from all the other biogenic tryptamines studied, having a marked behavioral effect with lack of interest in the surroundings, induction of palpebral ptosis, but no inhibition of spontaneous activity. It raised the level of emotionality in rats with conditioned fear response and, moreover, the effects of TNDT persisted for more than 10 days as opposed to an active period of only 2-3 hrs obtained with the other tryptamines. The possibility that TNDT may be produced by an inborn error enzyme formation in human psychotics is considered. 8 references. (Author abstract)

202773 Fechter, Laurence D. Dept. of Environmental Medicine, John Hopkins University, 615 N. Wolfe St., Baltimore, MD 21205 **The effects of L-dopa, clonidine, and apomorphine on the acoustic startle reaction in rats.** Psychopharmacologia (Berlin). 39(4):331-344, 1974.

Evidence for noradrenergic involvement in the elaboration of the acoustic startle reaction is presented. Within-subject experiments demonstrated that an amine-depleting dose of reserpine enhanced the level of the startle reaction and that this effect was reversed by the catecholamine precursor, L-Dopa. Chemical assays suggested a correlation between the accumulation of noradrenaline and reversal of reserpine effects. Administration of the noradrenaline receptor stimulating agent, clonidine produced marked reductions in startle amplitude reducing the response far below normal values in reserpinized subjects. By contrast, the dopamine receptor stimulating agent, apomorphine did not alter the response. None of the pharmacological agents used was found to alter the inhibition of the startle reaction which results from the presentation of neutral stimuli (prepulses) shortly before reflex elicitation. The data suggest that noradrenaline and serotonin have partially antagonistic control over the startle reaction. 16 references. (Author abstract)

202774 Creese, Ian; Iversen, Susan D. Johns Hopkins University School of Medicine, 725 North Wolfe Street, Baltimore, MD 21205 **The role of forebrain dopamine systems in amphetamine-induced stereotyped behavior in the rat.** Psychopharmacologia (Berlin). 39(4):345-357, 1974.

The caudate nucleus or the tuberculum olfactorium of the rat was lesioned by bilateral stereotaxic injection of 6-hydroxydopamine and the degree of dopamine depletion was assessed by a sensitive regional dopamine assay and revealed severe depletions in the lesioned areas. The locomotor response to a low dose of d-amphetamine was not modified by either lesion. However, the stereotypy response to a high dose of amphetamine was abolished by the caudate lesion. The stereotypy response was not modified by lesion to the tuberculum olfactorium. Neither lesion abolished the stereotypy response to apomorphine. The results therefore demonstrate that amphetamine is an indirect sympathomimetic agent and further emphasize the critical role of the dopaminergic nigrostriatal pathway in amphetamine-induced stereotypy. 32 references. (Author abstract)

202779 Decsi, L.; Nagy, Julia. Institute of Pharmacology, Medical University, 7643 Pecs, Hungary **Chemical stimulation of the amygdala with special regard to influence on the hypothalamus.** Neuropharmacology (Oxford). 13(12):1153-1162, 1974.

Four different parts of the amygdala were chemically stimulated in waking cats, and the effects on gross behavior, spontaneous electrical activity of the brain as well as carbachol-induced hypothalamic emotional reaction were studied. Carbachol stimulation in all regions investigated had no effect on gross behavior. It caused a shift towards high amplitude slow wave activity in the electroencephalograph (EEG) pattern and inhibited, in a dose-related manner, the rage reaction evoked by direct carbachol stimulation of the anteriomedial hypothalamus. The effects were seen after injecting carbachol into the central or lateral part of the amygdaloid complex, while stimulation of the anterior or basal amygdala was fully ineffective. The effect of carbachol from the central amygdala was blocked by a previous topical application of atropine. Nicotine inhibited the rage reaction only from the lateral part of the amygdala. Noradrenaline, when injected into the lateral or basal amygdala, caused very mild sedation, exhibited EEG effects similar to those seen after carbachol application in the central or lateral part of the amygdala and also inhibited the hypothalamic rage reaction. This action probably was a beta receptor effect, for isoprenaline was also effective while phenylephrine and dopamine were not. 21 references. (Author abstract modified)

202780 Beleslin, D. B.; Grbovic, Leposava; Radmanovic, B. Z. Department of Pharmacology, Medical Faculty, Beograd 11105, Yugoslavia **The pharmacology of gross behavioural effects of cholinomimetic substances injected into the cerebral ventricles of unanaesthetized cats: evidence for central muscarinic mediation.** Neuropharmacology (Oxford). 13(12):1163-1169, 1974.

Choline esters (acetylcholine, methacholine and carbachol) as well as substances with a peripheral muscarinic type of action, such as pilocarpine and arecoline, injected intraventricularly to unanesthetized cats, evoked emotional behavior, autonomic changes, motor phenomena and clonic-tonic convulsions. The gross behavioral effects of various single doses of these agents were dose dependent. Of choline esters and substances with peripheral muscarinic type of actions that were administered, carbachol was the most potent. The emotional behavior effects after pilocarpine were slight and few in number in comparison with those produced by choline esters. Atropine and scopolamine, injected intraventricularly, abolished the emotional behavior, autonomic changes, motor phenomena and clonic-tonic convulsions of intraventricularly-injected choline esters, while only scopolamine antagonized the gross behavioral effects of pilocarpine and arecoline. It is concluded that choline esters, applied intraventricularly to unanesthetized cats, elicit excitant behavioral phenomena by an action on central muscarinic cholinoceptive sites. 34 references. (Author abstract modified)

202781 Beleslin, D. B.; Samardzic, Ranka; Malobabic, Z. S. Department of Pharmacology, Medical Faculty, Beograd 11105, Yugoslavia **An analysis of the gross behavioural changes induced by tetraethylammonium and a comparison with other substances affecting the autonomic and central nervous system after intraventricular injections to conscious cats.** Neuropharmacology (Oxford). 13(12):1171-1177, 1974.

Tetraethylammonium (TEA) injected intraventricularly in conscious cats caused emotional behavior, autonomic changes

and motor phenomena, as well as clonic-tonic convulsions. The gross behavioral effects of various single doses of TEA are dose dependent. Atropine and scopolamine, when injected intraventricularly, abolished the emotional behavior, but did not antagonize the autonomic and motor changes nor the clonic-tonic convulsions of intraventricular TEA. Ganglionic and neuromuscular blocking agents, adrenergic blocking drugs, a 5-hydroxytryptamine antagonist, an antihistamine, antiepileptic drugs, calcium chloride, magnesium chloride, chlorpromazine, glycine and noradrenaline, failed to block the gross behavioral effects of intraventricular TEA. It is concluded that the emotional behavior caused by intraventricular injections of TEA in conscious cats is mediated through central muscarinic cholinoceptive sites, probably by enhanced release of acetylcholine. The autonomic changes, motor phenomena and convulsions elicited by TEA are most likely the consequence of its direct actions on the nerve cells. 26 references. (Author abstract modified)

202788 Asher, I. M.; Aghajanian, G. K. Department of Pharmacology, Yale University School of Medicine, New Haven, CT 06508 **6-Hydroxydopamine lesions of olfactory tubercles and caudate nuclei: effect on amphetamine-induced stereotyped behavior in rats.** Brain Research (Amsterdam). 82(1):1-12, 1974.

Amphetamine-induced stereotyped behavior in rats has been used as an animal model of psychosis. Much evidence has indicated that this behavior is mediated by an effect of amphetamine on central nervous system dopamine. There are two distinct ascending dopamine pathways (i.e. nigro striatal and mesolimbic). Attempts to determine which of these two pathways mediates amphetamine-induced stereotypy have been inconclusive. In an effort to clarify this question, 6-hydroxydopamine lesions were made in the forebrain terminal areas of the two pathways in rats and the response of the animals to the subsequent administration of D-amphetamine and apomorphine was observed. The brains were then analyzed by histofluorescence microscopy to determine the boundaries of dopamine-depleted areas. The results indicate that amphetamine-induced stereotyped behavior is mediated by the dopamine projection to the head of the caudate nucleus. The mesolimbic dopamine pathway does not appear to be necessary for amphetamine-induced stereotypy. 36 references. (Author abstract)

202792 Costall, Brenda; Naylor, Robert J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, Yorkshire, England **Stereotyped and circling behaviour induced by dopaminergic agonists after lesions of the midbrain raphe nuclei.** European Journal of Pharmacology (Amsterdam). 29(2):206-222, 1974.

The effects of electrolytic lesions of the midbrain nuclei were used as indicators for the role of 5-hydroxytryptamine in the mediation of stereotyped and circling behavior observed after peripherally-administered dopaminergic agonists, apomorphine, D-amphetamine and L-amphetamine, methylphenidate and piribedil, and intrastriatal dopamine in the rat. Lesions of the medial and/or dorsal raphe nuclei reduced the stereotypic effects of all agents, especially apomorphine. Following asymmetric lesions of the medial raphe nucleus all agents, excepting piribedil, enhanced or induced a contralateral circling behavior in a dose-dependent manner. Lesions of the raphe nuclei reduced the stereotypic effectiveness of bilateral intrastriatal dopamine but did not significantly modify the asymmetries induced by unilateral intrastriatal dopamine, although the normal effectiveness of haloperidol in enhancing these dopamine asymmetries was abolished by the raphe lesions. The medial and dorsal raphe nuclei play an important role in the development of stereotyped behavior and the medial nucleus is also important for the control of circling behavior. 32 references. (Author abstract modified)

202793 Price, Marion T. C.; Fibiger, Hans C. Department of Psychiatry, University of British Columbia, Vancouver, British Columbia, Canada **Apomorphine and amphetamine stereotypy after 6-hydroxydopamine lesions of the substantia nigra.** European Journal of Pharmacology (Amsterdam). 29(2):249-252, 1974.

Bilateral lesions of the substantia nigra with 6-hydroxydopamine abolished amphetamine-induced stereotypy but potentiated the stereotypic effects of apomorphine. The lesions reduced neostriatal dopamine to less than 2% of the control value. The data point to the questionable value of attempting to interpret the behavioral consequences of lesions to central catecholamine neurons in the absence of either biochemical or histochemical verification. The data support the view that amphetamine acts indirectly by increasing the release of catecholamines while apomorphine directly stimulated central dopamine receptors. 15 references. (Author abstract modified)

202794 Ranje, Christer; Ungerstedt, Urban. Department of Histology, Karolinska Institutet, Stockholm, Sweden **Chronic amphetamine treatment: vast individual differences in performing a learned response.** European Journal of Pharmacology (Amsterdam). 29(2):307-311, 1974.

In a study of chronic amphetamine treatment, animals were taught to swim an underwater Y-maze. After learning was completed, swim time and number of errors was recorded during treatment with d-amphetamine. Repeated exposure to d-amphetamine caused a pronounced difference in the performance between individual animals: some animals behaved as controls while others showed progressively worse performance with each dose of d-amphetamine even when the doses were spaced 12 days apart, indicating the priming effect of a single treatment. The results are discussed in relation to conflicting results in the literature concerning the effect of chronic amphetamine treatment. 17 references. (Author abstract modified)

202802 Kamei, Chiaki; Masuda, Yoshinobu; Shimizu, Masanao. Department of Pharmacology, Research Laboratories, Dainippon Pharmaceutical, Co., Ltd., Suita-shi, Osaka, Japan **Effects of psychotropic drugs on hypothalamic self-stimulation behavior in rats.** Japanese Journal of Pharmacology (Kyoto). 24(4):613-619, 1974.

Effects of psychotropic drugs on intracranial self-stimulation behavior were investigated in rats with chronic electrodes implanted in the lateral posterior hypothalamus. Major tranquilizers such as chlorpromazine, levomepromazine, haloperidol, clozapine and oxypertine caused a selective depression of self-stimulation at nondebilitating doses, and a dose-response relationship was also observed. Diazepam depressed this behavior at a dose much larger than that impairing rotarod performance. Chlordiazepoxide failed to depress self-stimulation even at 50mg/kg, and rather slightly facilitated this behavior at smaller doses. The mode of action of pentobarbital was similar to that of diazepam. Antidepressants, imipramine and amitriptyline depressed this behavior only at doses larger than those which significantly impaired coordinated motor activity. Methamphetamine rather facilitated self-stimulation at 0.5-1mg/kg, but depressed it at 5mg/kg. It is concluded that hypothalamic self-stimulation is not selectively depressed by major tranquilizers. 13 references. (Author abstract)

202803 Kulkarni, S. K.; Dandiya, P. C. Department of Pharmacology, S.M.S. Medical College, Jaipur 302004, Rajasthan, India **A preliminary report on the action of imipramine and antiparkinsonian agents on the open field behaviour of rats.** Japanese Journal of Pharmacology (Kyoto). 24(5):809-810, 1974.

The simple and complex stereotyped behavior of rats in the open-field situation were examined employing benztropine and imipramine. Although benztropine produced a high degree of complex stereotype behavior, the extreme forms of stereotypy that are observed with higher doses of amphetamine, however, could not be produced by benztropine. The complex stereotypy due to benztropine has been explained via the dopamine-reuptake-inhibiting property of the drug. The failure of imipramine to modify the individual or the combined action of benztropine and l-dopa suggests that both benztropine and imipramine have different affinities for norepinephrine and dopamine neurons. Pretreatment with imipramine or benztropine selectively reversed the effects of 6-hydroxydopamine, which is known to be taken up by both norepinephrine and dopamine neurons, on ambulation and rearing respectively thus indicating the differences in the affinities of imipramine and benztropine for norepinephrine and dopamine neurons as simple and complex stereotypies were mediated by brain noradrenergic and dopaminergic systems respectively. 10 references.

202806 Ahlenius, Sven; Brown, Roger; Engle, Jorgen; Lundborg, Per. Department of Pharmacology, University of Goteborg, Goteborg, Sweden **Learning deficits in 4-week-old offspring of the nursing mothers treated with the neuroleptic drug penfluridol.** Navnyn-Schmiedeberg's Archives of Pharmacology (Berlin). 279(1):31-37, 1973.

The acquisition of a conditioned avoidance response (CAR) was investigated in rats of nursing mothers given penfluridol 1.0mg/kg on days 1, 3 and 5 after delivery. The male litter mates were tested for CAR acquisition 4 weeks after birth. The animals whose mothers had received penfluridol were markedly inferior in the CAR acquisition than rats of mothers given glucose. Rats of penfluridol-treated mothers were found to be heavier than those of glucose-treated mothers when weighed at 8 weeks old. There was no difference between the groups at 4 weeks old. The possibility that penfluridol interacts with the development of catecholamine mechanisms in the brain at a sensitive developmental period, and thereby influences later performance, is discussed. 27 references. (Author abstract)

202863 Stille, G.; Lauener, H. 497 Bad Oeynhausen, Brandenburger Strasse 25, Germany /**The effects of neuroleptic agents in the chronic pharmacological experiment.**/ Die Wirkung von Neuroleptika im chronischen pharmakologischen Experiment. Arzneimittel-Forschung (Aulendorf). 24(9):1292-1294, 1974.

Tolerance formation in rats was studied after the application of haloperidol, fluphenazine, and loxapine. Doses of 2mg/kg were administered orally each day up to 4 weeks. After only 1 week of treatment, a lessening of the protective effect against apomorphine-induced chewing was noted, and there was a marked reduction in the rise of homovanillic acid, which can usually be observed in the corpus striatum after the administration of neuroleptic drugs. With regard to catalepsy, the reaction differed from product to product. The electroencephalogram changes typical of neuroleptic agents in rats were also an indication of tolerance. 15 references. (Journal abstract modified)

202864 Kreiskott, H. Neuropharmakologische Abteilung, Knoll AG, Chemische Fabriken, 67 Ludwigshafen/Rhein, Germany /**Behavioral changes induced by psychotropic substances in experimental animals.**/ Verhaltensanderungen durch psychotrope Substanzen bein Versuchstieren. Arzneimittel-Forschung (Aulendorf). 24(9):1294-1297, 1974.

The effect of psychotropic substances in animals is described in terms of motor reactions and specific drives. Numerous parameters were obtained from the pattern of effect and intoxication in the white mouse. In separate experimental arrangements, the induction or inhibition of food intake, predatory behavior, motor activity, preening, convulsions, catalepsy, defense, as well as aggression by drugs were tested in different species. The dependence on morphine together with the syndrome of withdrawal in mammals shows that the results can be largely applied to man. 60 references. (Journal abstract modified)

202968 Scheuer, Cynthia; Moore, John N. Florida Atlantic University, Boca Raton, FL 33432 **Breakdown of stimulus control by d-amphetamine.** Physiological Psychology. 2(4B):427-430, 1974.

Results of a series of experiments designed to determine the effects of d-amphetamine sulfate on behavior regulated by internal and external stimulus control in rats are reported. Six albino rats served as subjects. A two-bar switching schedule was utilized so that both perseveration and premature switching could be analyzed. All subjects, in all experiments, demonstrated increased variability under all drug contingencies. Both internal and external stimulus control broke down after the administration of the drug and was marked by general perseveration on the first bar. Transition behavior regulated by internal cues resulted in premature switching. 5 references. (Author abstract)

202969 Johansson, Jan O; Henriksson, Bengt G.; Jarbe, Torbjorn U. C. University of Uppsala, Slottsgrand 3, S-752 20 Uppsala, Sweden **Effects of delta8-THC on dissociation of conditioned avoidance responding in tolerant and nontolerant rats.** Physiological Psychology. 2(4B):431-432, 1974.

The effects of delta8-tetrahydrocannabinol (delta8-THC) on the dissociation of conditioned avoidance responding (CAR) in tolerant and nontolerant rats were studied. Previous laboratory work with delta8-THC on CAR has indicated a possible symmetrical dissociative effect on CAR retention. Results indicate that delta8-THC (15mg/kg) induces asymmetrical dissociation given that rats are made tolerant to the acutely disruptive effects of the drug. After a 15-day drug-free period, previously tolerant animals also showed disruption of established CAR. 11 references. (Author abstract modified)

202980 Meliska, Charles J.; Fitzpatrick, Kevin W.; Rosine, Jerry E. Monmouth College, Monmouth, IL 61462 **Effects of nicotine on spontaneous locomotor activity in rats having high and low basal activity levels.** Physiological Psychology. 2(4B):487-489, 1974.

The effects of nicotine on spontaneous locomotor activity in rats having high and low basal activity levels were studied. Two groups of six rats each, preselected for high and low rates of spontaneous wheelrunning activity, were tested immediately following injections of either distilled water or nicotine hydrogen tartrate. At 0.10, 0.20, 0.40 and 0.80mg/kg, nicotine depressed wheelrunning significantly in the high-activity subjects during the first 20 minutes after the injection. The performance of the low-activity subjects was not signifi-

cantly affected by any dose of the drug. No evidence of tolerance development to the depressant actions of the drug was obtained. 8 references. (Author abstract modified)

202983 Nyby, John; Belknap, J. K.; Thiessen, D. D. Univ. of Texas at Austin, Austin, TX 78712 **The effects of d- and l-amphetamine upon hoarding behavior and feeding in the Mongolian gerbil (Meriones unguiculatus).** Physiological Psychology. 2(4B):497-499, 1974.

The effects of d-amphetamine and l-amphetamine upon hoarding behavior and feeding in the Mongolian gerbil (Meriones unguiculatus) were examined. D-amphetamine was found to be more potent than l-amphetamine in suppressing both food hoarding and feeding behavior in the gerbil. Implications of these findings for a physiological explanation of rodent food hoarding are discussed. 27 references. (Author abstract modified)

202987 Cooper, Sidney; Coon, Kathleen; Mejta, Cheryl; Reid, Larry. Bradley University, Peoria, IL 61606 **Methods of deconditioning persisting avoidance: amphetamine, chlorpromazine, and chlordiazepoxide as adjuncts to response prevention.** Physiological Psychology. 2(4B):519-522, 1974.

The effects of amphetamine, chlorpromazine and chlordiazepoxide in deconditioning persisting avoidance in rats were studied. Rats were given extended avoidance training in an automated one way avoidance chamber, a chamber with a retractable ledge. After training and footshock termination, some rats were prevented from responding by being trapped on the footshock grid with the ledge removed. During this response prevention, rats were under the influence of either amphetamine, chlorpromazine, chlordiazepoxide, or a placebo. Subsequently, rats were tested for continuance of responding when footshock no longer occurred. Only response prevention with amphetamine reduced persisting avoidance responding compared to no treatment. 16 references. (Author abstract modified)

203166 Quinn, Clifton Pegues. University of Pennsylvania, Philadelphia, PA **Effects of amphetamine and and chlorpromazine upon observing responses in rats. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-22896 HC$12.50 MF$4.00 194 p.

The effects of d-amphetamine, having generally opposite physiological and behavioral effects as those of drugs such as chlorpromazine, on observing responses in rats were studied. Also, the generality of previously-found effects of chlorpromazine in pigeons was tested by using a different species. Results for d-amphetamine were characterized by a decrease in the ratio of stimulus-producing to food-producing responses. Chlorpromazine had the opposite effect. A concept of stimulus-producing responses as a variety of alternative behavior was supported, mediated by nonadrenergic neural systems, inhibited by adrenergic systems of reward, and therefore facilitated when primary reward occurs infrequently. (Journal abstract modified)

203204 Panaccio, Lucien; Tetreault, Leon. no address /A **comparative study of the hypnotic properties of flurazepam (30 mg), secobarbital (100 mg), and of placebo among four types of psychotic insomniacs./** Etude comparative des proprietes hypnotiques du flurazepam (30 mg), du secobarbital (100 mg) et du placebo chez quatre types d'insomniaques psychotiques. Union Medicale du Canada (Montreal). 101:2420-2425, 1972.

The hypnotic effects of flurazepam (30mg), secobarbital (100mg) and placebo were compared on four groups of psychotic insomniacs. The 61 subjects of the experiment were classed according to the following four types of insomnia: vesperal, night, morning and mixed insomniacs. The sequence of administration of the three drugs to each patient was randomized and a double-blind technique was used. The seven rated sleep parameters were: duration and quality of induction, duration and quality of sleep, waking periods, sleep disturbing dreams and finally awakening and following morning. In all cases, intersubject differences were significant. Interaction between the medication and the types of insomnia could not be demonstrated for any of the seven parameters. Patients suffering from morning insomnia showed a better quality induction period, compared to the group presenting mixed insomnia. Both hypnotic drugs caused a longer duration of sleep in all subjects, but only flurazepam was shown to be significantly superior to placebo. Quality of sleep was also favorably influenced by flurazepam: in fact, flurazepam was demonstrated to be preferable to both placebo and secobarbital. 5 references. (Author abstract modified)

203520 Oliverio, Alberto. Laboratorio di Psicobiologia e Psicofarmacologia CNR, 1, via Reno, 00198 Rome, Italy **Genotype-dependent electroencephalographic, behavioral and analgesic correlates of morphine: an analysis in normal mice and in mice with septal lesions.** Brain Research (Amsterdam). 83(1):135-141, 1975.

Two strains of inbred mice (C57BL/6J and DBA/21) were implanted with epidural cortical electrodes to determine: (1) if the electroencephalographic (EEG) responses to morphine are also modulated by genetic factors; (2) if morphine-induced changes in brain electrical activity are correlated to the differences in locomotor and analgesic responses evident between the strains of mice; and (3) if lesion of the septum, which results in a reduction of the analgesic effects of morphine, also affects the EEG response to the opiate. The findings suggest that: (1) the EEG responses to morphine are genetically determined; (2) the septal area is implicated in morphine-induced analgesia but not in the locomotor responses or in the brain electrical responses to the opiate; (3) the EEG alterations induced by morphine do not seem to be directly connected with the analgesic properties of the drug. 17 references. (Author abstract modified)

203521 Danscher, G.; Fjerdingstad, E. J. Institute of Anatomy, University of Aarhus, Aarhus, Denmark **Diethyldithiocarbamate (antabuse): decrease of brain heavy metal staining pattern and improved consolidation of shuttle box avoidance in goldfish.** Brain Research (Amsterdam). 83(1):143-155, 1975.

Diethyldithiocarbamate (DEDTC), a chelating compound considered to be the active metabolite of the antialcoholic drug Antabuse, abolishes the Timm staining for heavy metals in the brains of goldfish kept in solutions of DEDTC for periods of 1 hour. The effect of a single treatment is reversible, and its magnitude and duration dependent on the concentration of DEDTC. Fish exposed to DEDTC solutions immediately after a first training session in a shuttle box avoidance task were found to perform significantly better in a second session 24 hours later. DEDTC treatment 24 hours before the first session, or with a delay of several hours after the first session, was without effect. These results suggest that DEDTC has a specific facilitating effect on memory consolidation. 40 references. (Author abstract)

203572 Squire, Larry R.; Kuczenski, Ronald; Barondes, Samuel H. Dept. of Psychiatry, Univ. of California, San Diego School of Medicine, La Jolla, CA 92037 **Tyrosine hydroxylase inhibition by cycloheximide and anisomycin is not responsible for their amnesic effect.** Brain Research (Amsterdam). 82(2):241-248, 1974.

A study with mice to determine if the amnesic effect of cycloheximide could be due to reduction of norepinephrine synthesis rather than to inhibition of protein synthesis required for long-term memory is reported. Results show that: (1) amnesic doses of cycloheximide and anisomysin, two protein synthesis inhibitors, produced measurable depression of tyrosine hydroxylase activity although much of the depression may be due to isotope dilution rather than true inhibition, and (2) alpha-methyl-p-tyrosine, a competitive inhibitor of tyrosine hydroxylase, in doses which depressed tyrosine hydroxylase activity as much or more than either cycloheximide or anisomycin, did not affect memory. Therefore the effect of protein synthesis inhibitors on brain tyrosine hydroxylase is not sufficient to explain their amnesic effect. 23 references. (Author abstract modified)

203579 Lanier, Linda Patia; Petit, Ted LaRue; Isaacson, Robert L. Dept. of Psychology, Univ. of Florida, Gainesville, FL 32611 **Protection against effects of brain damage by catecholamine depletion is test dependent.** Brain Research (Amsterdam). 82(2):374-377, 1974.

An attempt to determine how wide a range of behavioral effects produced by experimental brain damage in rats would be attenuated by treatment with alpha-methyl-p-tyrosine (AMT) prior to surgery is reported. Intraperitoneal injections of AMT were given to one group of rats (hippocampally damaged and AMT treated) while another group served as control (AMT treated). Results indicate that the administration of AMT before hippocampal destruction failed to affect hyperactivity in the open field produced by the lesion, but it did not change performance in a passive avoidance task. This would indicate that test specific differences in recovery have been produced by the AMT administration rather than the global remission of all behavioral consequences of the brain damage. The data indicate that the benefits of AMT administration are test specific and are not a general remedy for all deficits produced by hippocampal damage. 9 references. (Author abstract modified)

204424 Kimishima, Kenjiro; Tanabe, Kyoko; Yamasaki, Michiyo; Shimabukuro, Takashi; Hanada, Yoshiyuki. Department of Pharmacology, Tottori University School of Medicine, Yonago, Japan **Central nervous action of L-Dopa.** Journal of the Yonago Medical Association (Yonago). 25(2):161-167, 1974.

Effects of L-dopa combined with 5-hydroxytryptophan (5-HTP) or dopa decarboxylase inhibitor (Ro4-4602) on the central nervous system of mice were studied. Findings indicate: 1) tremor induced by tremorine, harmine and harmaline was considerably inhibited by combined administration of L-dopa and 5-HTP; 2) inhibitory effects of drug-induced catalepsy and akinesia were scarcely observed in the concomitant use of L-dopa and 5-HTP; 3) tremorine-induced tremor was markedly inhibited by administration of L-dopa associated with Ro4-4602; 4) the most effective dose ratio of L-dopa to Ro4-4602 was 3-4:1. This combination demonstrated slight inhibition of catalepsy produced by major tranquilizers and no inhibition of bulbocapnine-induced akinesia. 11 references. (Author abstract modified)

204482 Peterson, Dale W.; Sparber, Sheldon B. Dept. of Pharmacology, Univ. of Minnesota, Minneapolis, MN 55455 **Increased fixed-ratio performance and differential d- and l-amphetamine action following norepinephrine depletion by intraventricular 6-hydroxydopamine.** Journal of Pharmacology and Experimental Therapeutics. 191(3):349-357, 1974.

A two part study which examined the long-term effects on operant behavior of a dose of 6-hydroxydopamine (6-OHDA) that depleted norepinephrine (NE) without affecting dopamine (DA) levels in the rat brain and which determined the effect of 6-OHDA-induced NE depletion on the behavioral action of d-amphetamine and l-amphetamine in order to further define the stereospecific effects of this drug is reported. The injection of 6-OHDA into rats trained to respond on a fixed-ratio 30 (FR 30) schedule of food reinforcement resulted in decreased response rates which returned to predrug rates after 8 days. The response rates gradually increased and remained greater for up to 156 days after the 6-OHDA treatment. The drug depleted hypothalamic and midbrain-striatal NE measured 1 week later but midbrain-striatal DA was unchanged. After 5.5months, NE levels had partially recovered and the recovery was correlated with increased response rates. The suppression of the FR responding by d-amphetamine was not altered by the 6-OHDA. When l-amphetamine was given to the same rats, the behavioral suppression was attenuated in the group that had received 6-OHDA. Results suggest a greater importance of NE in some of the operant behavioral actions of l-amphetamine than of d-amphetamine. 36 references. (Author abstract modified)

204733 Keyes, Joseph B. Louisiana State University and Agricultural and Mechanical College **The effect of ACTH and amphetamine on ECS-produced amnesia. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-24783 HC$12.50 MF$4.00 45 p.

The effect of ACTH and amphetamine on electroconvulsive shock (ECS) produced amnesia in rats was investigated in two experiments. In experiment one, subjects were trained on a one-way active avoidance task to a criterion of two avoidances out of any three consecutive trials. Upon reaching criterion, they were removed from the apparatus and given either ECS or no treatment. Six hours later, they received retrieval treatments of footshock, ACTH injection, saline injection, or amphetamine injection and given a retention test trial and retraining 24 or 72 h after retrieval treatment. ECS produced apparent amnesia for the task; amnesia was eliminated by a retrieval treatment of noncontingent footshock or ACTH injection. Saline and amphetamine were not effective recovery agents. Effects lasted for at least 72 h. In experiment two, subjects were trained and given ECS or no treatment. They then received a retention trial and retraining either 24 or 168 h after treatment. Recovery from ECS produced amnesia did not spontaneously occur for at least 168 h after treatment. (Journal abstract modified)

205335 Crow, Lowell T.; Edelbrock, Craig. Western Washington State College, Bellingham, WA 98225 **Stimulus properties of sympathomimetic and sympatholytic drugs.** Bulletin of the Psychonomic Society. 4(6):575-577, 1974.

Albino rats were trained in shuttle box avoidance under one of the following three drug conditions: Sus-Phrine (S), D.H.E.-45 (D), or placebo (P). Twenty-four hours later the animals were tested for retention in the same or a different drug state. No evidence was found for drug sequence effect although the D group exhibited significantly more avoidances. An operant conditioning procedure yielded results supporting discriminative stimulus properties of D.H.E.-45. The results are discussed as they relate to the discriminative control of

behavior through stimuli of an autonomic character. 10 references. (Author abstract)

205418 Houser, Vincent P. Psychotropic Drug Laboratory, Veterans Administration Hospital, Perry Point, MD 21902 **The alteration of aversive thresholds after chronic administration of two tranquilizing agents.** Behavioral Biology. 12(3):383-392, 1974.

A major tranquilizer, chlorpromazine, and a minor tranquilizer, chlordiazepoxide were administered to squirrel monkeys performing under a titration schedule to ascertain their effects upon aversive thresholds. Both agents reliably raised the aversive threshold to electric shock, but chlorpromazine was more potent in this regard. Chlordiazepoxide was able to augment the aversive threshold to moderate levels only under the middle range of doses tested, while chlorpromazine was able to raise the threshold to maximum levels under the 0.25mg/kg dosage. These results were interpreted to suggest that chlordiazepoxide may have analgesic properties at moderate doses, while chlorpromazine may raise the aversive threshold by interfering with the execution of the operant response. 10 references. (Author abstract)

205432 Glick, Stanley D.; Jerussi, Thomas P.; Waters, Donald H.; Green, Jack P. Department of Pharmacology, Mount Sinai School of Medicine, City University of New York, NY **Amphetamine-induced changes in striatal dopamine and acetylcholine levels and relationship to rotation (circling behavior) in rats.** Biochemical Pharmacology (Oxford). 23(22):3223-3225, 1974.

Amphetamine-induced changes in striatal dopamine and acetylcholine levels and their relationship to rotation behavior in rats were examined. The results indicate that there is a normal imbalance in the content of dopamine in the left and right striati and the potentiation of this imbalance is associated with rotation. The amphetamine potentiated imbalance is a function of the same mechanism responsible for amphetamine-induced depletion of striatal dopamine since the imbalance was correlated with the depletion. 10 references.

205464 Hara, T. Sagamihara, Japan **Experimental studies on the psychical episodes of epilepsy.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):712-713, 1973.

A paper presented at the 8th International meeting of Electroencephalography and Clinical Neurophysiology reported experimental studies on the psychical episodes of epilepsy. Systemic administration of N-methyl-d-aspartic acid induced continuous desynchronization and intermittent seizure discharges in the hippocampal electroencephalogram (EEG) of cats. These EEG changes lasted for 1-2 hrs and, in this condition, the threshold of the rage reaction produced by electrical stimulation of the ergotropic zone of the brainstem was lowered. After giving the drug, animals with a small irritative lesion in the ergotropic zone became restless and demonstrated effective-defensive behavior. It is concluded that the brain mechanisms underlying the episodic psychical states of epilepsy may be attributable to the combination of activation of the epileptogenic foci of the brainstem and the dysfunction of the hippocampus. (Author abstract modified)

205588 Poschlova, N.; Krsiak, M.; Ostrovskaya, R. U. Czechoslovak Academy of Sciences, Albertov 4, 128 00 Praha 2, Czechoslovakia **Effect of sodium gamma-hydroxybutyrate on isolation-induced aggressivity in mice.** Activitas Nervosa Superior (Praha). 16(3):172, 1974.

At the 16th Annual Psychopharmacological Meeting, the effect of sodium gamma-hydroxybutyrate (GHB) on isolation-induced aggressivity in mice was reported. The lower dose of GHB did not produce significant changes, while the higher dose of GHB lowered all behavioral activities. GHB thus decreased aggressivity of the isolated mice in a comparatively low dose which did not produce general sedation of animals. Also the isolation-induced timidity was reduced by 50mg/kg of GHB. GHB thus seems to possess a comparatively specific tranquillizing activity. 3 references.

05 TOXICOLOGY AND SIDE EFFECTS

199255 Vugman, I.; Rodrigues, J. M. Gomez. Dept. de Morfologia, Faculdada de Medicina, Caixa postal 301, 14100 - Ribeirao Preto, S. P., Brazil **The inhibitory effect of toluidine blue and methylene blue on rat mast cell damage by promethazine, chlorpromethazine and chlorpromazine. Its reversal by glucose.** Experientia (Basel). 30(10):1178-1180, 1974.

The inhibitory effect of toluidine blue and methylene blue on rat mesentery mast cell damage by phenothiazine compounds with antihistamine activity (promethazine, chlorpromethazine, and chlorpromazine) and its reversal by glucose are described. The antienzymatic mechanism postulated to explain the inhibitory effect of these stains is substantiated. 10 references.

199898 Littleton, J. M. Department of Pharmacology, King's College, Strand, London W.C. 2, England **Dual mechanism of amphetamine toxicity in mice: relationship to brain catecholamines.** Acta Pharmacologica et Toxicologica (Kobenhavn). 34(1):92-96, 1974.

In a study of the relationship of amphetamine toxicity in mice to brain catecholamines, brain noradrenaline (NA) and dopamine (DA) concentrations were estimated by the fluorimetric method. Grouped mice showed a greater depletion of brain noradrenaline than isolated mice and this depletion occurred only at low doses of amphetamine. There was no significant difference in catecholamine depletion at high amphetamine doses between environmentally stressed and nonstressed mice. It is suggested that low dose amphetamine toxicity is related to the noradrenaline-depleting properties of amphetamine, whereas high dose toxicity may be related to activation of the central dopaminergic systems, possibly by direct receptor mechanisms. 9 references.

199912 Barzaghi, F.; Fournex, R.; Mantegazza, P. L. F. Maestretti Research Laboratories, Milan, Italy **Pharmacological and toxicological properties of clobazam (1-phenyl-5-methyl-8-chloro-1,2,4,5-tetrahydo-2,4-diketo-3H-1,5-benzodiazepine), , a new psychotherapeutic agent.** Arzneimittel-Forschung (Aulendorf). 23(5):683-686, 1974.

1-Phenyl-5-methyl-8-chloro-1,2,4,5-tetrahydro-2,4-diketo-3H-1,5-benzodiazepine (clobazam), a new type of benzodiazepine compound with the nitrogen atoms in the heterocyclic ring in position 1,5 instead of 1,4 was examined in mice. The drug was shown to possess sedative effect at much lower doses than those producing ataxia. It depressed spontaneous motor activity, reduced exploratory behavior and potentiated both ethanol and hexobarbital induced sleep. The substance was also very active in preventing fighting in isolated mice and in the foot shock test; furthermore, it exhibited a marked anticonvulsant activity against metrazol, electric shock seizure and strychnine. In all these tests clobazam was more active than chlordiazepoxide. No significant autonomic or untoward cardiovascular effects were noted in cats. 11 references. (Author abstract modified)

200168 Krigman, Martin R.; Druse, Mary J.; Traylor, T. Dennis; Wilson, Marion H.; Newell, Lanny R.; Hogan, Edward L. Department of Pathology, University of North Carolina, School of Medicine, Chapel Hill, NC **Lead encephalopathy in the developing rat: effect on cortical ontogenesis.** Journal of Neuropathology and Experimental Neurology. 33(5):671-686, 1974.

The effect of lead intoxication on postnatal cortical ontogenesis was studied in the 30-day-old rat. Lead encephalopathy was induced in developing Long-Evans rats by adding lead carbonate (4%w/w) to the diet of nursing mothers immediately after delivery. Lead intoxication resulted in an overall reduction of gray matter which was characterized by an astrocytosis and by the preservation of the neuronal population. Growth and maturation of the neurons in the lead rats were altered. The neurons were smaller, and, more important, the proliferation of nurite processes in the neuropil was retarded. There was also an apparent reduction in the number of synapses per neuron. In terms of its biochemical and morphological features, lead intoxication does not affect the maturation of the synaptic complex. The apparent effect of lead intoxication on cortical development is one of retarded neuronal maturation. This defect in neuronal maturation is proposed to be a reduction in the dendritic field and a concomitant reduction in synaptic connections. 35 references. (Author abstract modifed)

202722 Nasello, Antonia G.; Astrada, Carlos A.; Ramirez, Oscar A. Departamento de Farmacologia, Universidad Nacional de Cordoba, Cordoba, Argentina **Effects on the acquisition of conditioned avoidance responses and seizure threshold in the offspring of amphetamine treated gravid rats.** Psychopharmacologia (Berlin). 40(1):25-31, 1974.

In a study of the effect of the acquisition of conditioned avoidance responses and seizure threshold, female rats with 30 to 70% of conditioned responses in an avoidance conditioning session in a Warner cage, were treated daily during pregnancy with 0.5mg/kg of d,l-amphetamine administered subcutaneously. They had been mated with males selected with the same criterion who received no treatment. The control group differed from the treated one in that females received the same volume of saline solution instead of the drug. Teratogenic effects of the drug were not observed and there were no differences in either the age of eyes or vaginal aperture or in growth rate determined by the weekly weight between offspring of treated and control mothers. The pups of amphetamine-treated mothers had better acquisition and retention of conditioned avoidance responses than those of control mothers when they were 90 days old but no difference was observed at the age of 45 days. Offspring of the treated group had a lower hippocampal seizure threshold than the control group. The relation between the mechanisms of learning and seizure are discussed in connection with potassium release by stimulation in the hippocampus. 26 references. (Author abstract)

204400 Fenner, Helmut; Neye, J.; Biamino, G. Freie Universitat Berlin, Fachbereich Pharmazie, 1 Berlin 33, Konigin-Luise-Str. 2/4, Germany /**Negative inotropic effects of tricyclic antidepressants on the isolated right ventricular papillary muscle of the cat.**/ Negative inotroper Effekt von tricyclischen Antidepressiva am isolierten rechtsventrikularen Papillarmuskel der Katze. Arzneimittel-Forschung (Aulendorf). 24(8):1098-1101, 1974.

Because of the importance of the cardiovascular side-effects of tricyclic antidepressants in their clinical use, the influence of several drugs on isolated papillary muscles of cats was studied. Within the group of structurally similar antidepressants, imipramine, dibenzepine and dimetacrine, striking differences in the influence on cardiac muscle mechanics can be demonstrated. The antiarrhythmic drug procainamide was compared with the antidepressants, and in therapeutic dose ranges no effect on myocardial contractility was found. These results demonstrate the significance of structure-activity relationships in cardiovascular side-effects and are useful for studies on left heart catheterization patients for a further evaluation of the influence of tricyclic antidepressants on hemodynamic parameters. 15 references. (Journal abstract)

204879 Ahtee, Liisa; Jounela, A. J.; Saarnivaara, Laila; Simola, Irma. Dept. of Pharmacology, University of Helsinki, Helsinki, Finland **Interactions of some analgesics and antidepressants with phenelzine or reserpine in the mouse.** Pharmacology (Basal). 12(1):39-47, 1974.

The effect of phenelzine on the toxicity of six narcotic analgesics and two tricyclic antidepressants was studied in rats. The interactions of these agents with reserpine were also tested. Phenelzine pretreatment increased the group toxicity (LD50) of pethidine and imipramine, tended to increase that of methadone but did not change the LD50 of alphaprodine, anileridine, piminodine, pentazocine and protriptyline. Methadone, pethidine, imipramine and protriptyline partially prevented reserpine-induced hypothermia while piminodine and pentazocine potentiated it. Results show that the interactions of methadone and pethidine with phenelzine or with reserpine can be similar to those of imipramine with phenelzine or reserpine. 15 references. (Author abstract modified)

06 METHODS DEVELOPMENT

198488 Barkov, N. K.; Zakusov, V. V. Laboratoriya farmakologii nervnoy sistemy, Institut farmakologii AMN SSSR, Moscow /**Methods of assessing psychopharmacological agents in experiments.**/ Metody otsenki psikhofarmakologicheskikh sredstv v eksperimente. Farmakologiya i Toksikologiya (Moskva). 36(6):730-739, 1973.

Many successful methods of evaluating the effectiveness of psychopharmacological agents are listed under four basic categories: influence on behavior; bioelectrical activity of the brain; biochemical structure of the nervous system; and vegetative and hormonal reactions. Specific methods mentioned include monitoring of motor activity, analgetic effectiveness, emotional behavior in animals, particularly aggressiveness, conditioned reflexes in animals, particularly those conditioned by food, running through mazes and self-stimulation, activity of biogenic amines, and body temperature. The implementation and relative effectiveness of each method is discussed in detail. The concluding recommendation that no one method of assessment should be relied upon exclusively is supported by examples in which registration of changes in bioelectrical activity did not correspond to registered changes in behavior. 190 references.

201491 Costa, E.; Guidotti, A.; Uzunov, P.; Zivkovic, B. Lab. of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Methods to study the in vivo regulation of cyclic nucleotides in hypothalamic nuclei, pituitary and pineal. (Unpublished paper).** Washington, D.C., NIMH, 1974. 3 p.

The sensitivity of measuring increases of 30,50-cyclic adenosine monophosphate (cAMP) content was evaluated as an index of postsynaptic stimulation in rat pituitary, pineal and

whole hypothalamus. Both cAMP and 30,50-cyclic guanosine monophosphate (cGMP) were measured in rats exposed to 4 degrees centigrade or injected with reserpine. The cAMP content increased in anterior and posterior pituitary but failed to change in the hypothalamus. The cGMP concentration in these tissues also failed to change. The detection of the phosphodiesterase activator appears to be a reliable and sensitive measure to assess the activation in various hypothalamic nuclei of the activation of synapses which function through adenylcyclase. Measurements of cAMP and cGMP lack the sensitivity required to study the involvement of selective synapses in the neuroendocrine regulation. The measurement of cAMP dependent and independent protein kinase activity and that of the phosphodiesterase activator can be used to study the mode and site of action of drugs that modify the regulation of fertility at synaptic level.

202465 Racagni, G.; Cheney, D. L.; Trabucchi, M.; Wang, C.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Measurement of acetylcholine turnover rate in discrete areas of rat brain.** Life Sciences (Oxford). 15(11):1961-1975, 1974.

The turnover rate of acetylcholine (ACh) was estimated in brainstem, two cortical areas and striatum of rat brain. The turnover was highest in the striatum, lowest in brainstem, and intermediate values were observed in limbic and occipital cortex. The highest ACh concentrations were measured in the striatum, those in the brainstem were intermediate but in the two cortical areas, the ACh concentrations were the lowest. The results of the turnover estimations with the finite difference methods yielded values similar to those obtained with the experimental procedure. Once the baseline was established, this method could be reliably used to estimate turnover rate using a single infusion time. The simplification would be very useful to compare ACh turnover rate in drug studies. 9 references. (Author abstract modified)

202944 Hoffmeister, F. Institut fur Pharmakologie, Farbenfabriken Bayer AG, Werk Elberfeld, 56 Wuppertal 1, Friedrich-Ebert-Strasse 217, Germany /**Ways of demonstrating and differentiating central nervous effects of drugs in animal experiments.**/ Moglichkeiten des Erkennens und der Differenzierung zentral-nervoser Wirkungen von Pharmaka im Tierversuch. Arzneimittel-Forschung (Aulendorf). 23(8a):1131-1136, 1973.

Methods to identify and differentiate the effects of drugs on the central nervous system by way of tests on animals are described, using mice, rats, cats, rabbits and monkeys. Methods suitable to pharmacological experimentation in the neurosciences and behavioral psychology are discussed, which include sleep and wakefulness control and vigilance, hypnotic effects, anticonvulsive effects, induced convulsion and catalepsy, aggression, reaction to pain and pleasure and the animals' attempts at self-administration of drugs, including the opiates, sedatives, analgesics, hypnotics, stimulants and pleasure-producing drugs.

204189 John, E. R.; Walker, P.; Cawood, D.; Rush, M.; Gehrmann, J. Brain Research Laboratories, Dept. of Psychiatry, New York Medical College, New York, NY 10029 **Factor analysis of evoked potentials.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(1):33-43, 1973.

Averaged responses recorded during 13 different postdrug and 11 different predrug control sessions were subjected to principal component factor analysis and the resulting components were rotated following a Varimax procedure. Averages computed under different doses of the same drug were described by similar regression equations, markedly different descriptions were obtained for the effects of different drugs, and the results from different cats were in good agreement. It is noted that the method employed will provide a reliable quantitative description of any set of brain states which an investigator chooses to define. 14 references. (Author abstract modified)

CLINICAL PSYCHOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

198081 Gershon, Samuel. New York University Medical Center, New York, NY **Psychopharmacology of the lithium ion.** Psychopharmacology Bulletin. 10(2):58, 1974.

Lithium's value as a preventative for mania, as a treatment and a preventative for the depressed phase of manic-depression, and as a treatment for schizoaffective illness is tested. Manic patients, schizoaffectives, recurrent depressives, schizophrenics, endogenous depressives, and outpatients suffering from premenstrual tension were the subjects, and rats are used in some aspects of the study. Lithium showed some promise as a treatment for premenstrual tension and chlorpromazine was superior to lithium in treating schizophrenics of the schizoaffective and other diagnostic subtypes. There is a higher incidence of neurological toxic effects with lithium among schizophrenics than among manic patients. Lithium does not appear to have significant therapeutic activity as an antidepressive agent in the treatment of certain types of depression. (Journal abstract modified)

198082 Prange, Arthur J., Jr. University of North Carolina, Chapel Hill, NC **Acceleration of antidepressants by thyroid hormone.** Psychopharmacology Bulletin. 10(2):58-59, 1974.

The effect of the thyroid hormone triiodothyronine (T3) on several antidepressants is being studied, to determine the drug combinations that are most effective in relieving the symptoms of depression and to define the biochemical basis for the hormones' therapeutic effect. Two groups of patients, are receiving imipramine only and one receiving imipramine in combination with T3, are tested for effects of such variables as sex, type of depression, dosage, and time schedule of T3, and combination of T3 with electric shock. It was shown that T3 and thyroid-stimulating hormone (TSH) strengthened the action of imipramine and contriptyline, chiefly in depressed women. Another experiment showed that rats and mice in a high CO2, low O2 environment have a higher death rate when treated with phenothiazines. (Journal abstract modified)

198086 Cunningham, Patricia C. Our Lady of the Lake College, San Antonio, TX **Long-term correlates of drug use in hyperkinesis.** Psychopharmacology Bulletin. 10(2):61, 1974.

The effects of long-term use of psychotropic drugs (amphetamine and methylphenidate) on hyperactive children are being studied. Psychometric measurements and case histories covering drug use are taken on all subjects. Information is gathered concerning the socioeconomic status of the children, family size, and parents' educational background. Parental attitudes toward drugs, discipline, and educational achievement are also studied. (Journal abstract modified)

198088 Klein, Donald F. Long Island-Jewish Hillside Medical Center, Glen Oaks, NY **Comparative drug effects in hyperkinetic children.** Psychopharmacology Bulletin. 10(2):62-63, 1974.

The relative efficacy of thioridazine, methylphenidate, thioridazine-methylphenidate combination, and placebo in hyperkinetic children was examined. Methylphenidate effects on psychological tests among children with learning disabilities but no behavioral dysfunction were analyzed for a preliminary sample of 48 subjects. On the Wide Range Achievement Test (WRAT), both reading and arithmetic scores were significantly improved by methylphenidate treatment after 4 weeks of treatment. After 12 weeks, the methylphenidate and placebo groups were no longer significantly different either on the reading or arithmetic scores of the WRAT. The Gray Oral Reading Tests was not sensitive to drug effect at any point. (Journal abstract modified)

198095 Gottschalk, Louis A. University of California, Irvine, CA **Psychoactive drug blood levels and clinical response.** Psychopharmcology Bulletin. 10(2):66, 1974.

The relationships between standard doses of certain psychoactive drugs such as thioridazine and the blood drug levels that these doses produce are studied. Following treatment, periodic evaluations are made of blood drug levels and of changes in the patients' clinical conditions using the Brief Psychiatric Rating Scale and by various measures of social adjustment and personal organization including content analysis scales applicable to speech samples. (Journal abstract modified)

198097 Malitz, Sidney. New York State Department of Mental Hygiene, Albany, NY **Plasma levels of imipramine and clinical outcome.** Psychopharmacology Bulletin. 10(2):66-67, 1974.

The extent and character of genetic and psychological variability and their influence on effectiveness of imipramine are studied. Patients with endogenous unipolar depression receive doses of phenylbutazone, which serve as a predictive measure for the metabolic handling of imipramine. Unimproved patients are then treated for 1 month with imipramine and periodically rated according to self-reports, therapists reports and blood samples. Objectives are to increase knowledge of the antidepressant and of depressive illness. (Journal abstract modified)

198106 Fisher, Seymour. Boston University School of Medicine, Boston, MA **Methodology of outpatient drug research.** Psychopharmacology Bulletin. 10(2):71-72, 1974.

Factors which will enable the research clinician to develop simpler and more reliable methods of evaluating new drugs with outpatients are discussed. Psychiatric outpatients, dental patients, and normal adults were given a tranquilizer or a placebo for 2 weeks and later received psychotherapy. The effect of a tranquilizer varied with the personality characteristics of both doctor and patient. Outpatients were grouped according to scores on a social aquiescence (SA) test. High SA outpatients improved with placebo and got worse with drug treatment, while low SA's improved with the drugs but not with placebo. The drug had no adverse effects on subsequent therapy. When chlordiazepoxide, secobarbital, and placebo were compared for their effects on anxiety, sedation was evident, but the drugs did not prevent anxiety. Low SA's consistently reported lower "tension-anxiety" while on a drug than on a placebo; high SA's did not notice any difference. (Journal abstract modified)

198119 Channabasavanna, S. M.; Aresh, B. Government Mental Hospital, Bangalore, India **Clinical trial of trimipramine (Surmontil).** Indian Practitioner (Bombay). 27(1):67-71, 1974.

The efficacy of drug therapy with trimipramine (Surmontil) in cases of endogenous depression, the depressive phase of manic-depressive illness, depressive psychosis, agitative

depression, and reactive depression, is discussed. Data were obtained from 40 cases receiving such therapy on an outpatient basis. Dosage varied with degree of symptomatology. The drug was useful in treating all types of depression, and not effective when disturbed sleep was the most distressing symptom. Considerable improvement was noticed after 45 days of drug intake, and most patients began showing improvement after 21 days. 5 references.

199386 Rascol, A.; Maurel, H.; David, J.; Layani, M. C.H.R. de Toulouse, Service de Consultations de Neurologie, Toulouse, France /**Preliminary clinical results of a new nontricyclic antidepressant: oxaflozane (1766 Cerm).**/ Premiers resultats cliniques d'un nouvel antidepresseur non tricyclique: "l'oxaflozane" (1766 Cerm). Therapie (Paris). 29(1):95-99, 1974.

Preliminary results in clinical trials of oxaflozane, 2-(3-trifluoromethyl)-4-isopropyltetrahydro-1,4-oxazine, a nontricyclic antidepressant, are reported. The tolerance for the drug was good, with orthostatic hypotension sometimes noted during perfusion of the compound which was easily controlled by decubitus. The compound is quite effective in melancholic depressives, showing a 70% amelioration rate, with clinical improvement occurring within 48 hours. The percentage of positive results with neurotic depressives was also high; the most responsive condition to treatment with oxaflozane is psychasthenic depression. 3 references. (Journal abstract modified)

199632 Sack, Robert L.; Goodwin, Frederick K. Dept. of Psychiatry, Stanford University, School of Medicine, Palo Alto, CA **Inhibition of dopamine-beta-hydroxylase in manic patients: a clinical trial with fusaric acid.** Archives of General Psychiatry. 31(5):649-654, 1974.

Behavioral effects of fusaric acid, a specific inhibitor of dopamine-beta-hydroxylase (DBH), were evaluated under double-blind conditions in manic patients. Inhibition of DBH selectively decreases central norepinephrine (NE) without a decrease in dopamine and thus provides a test of the NE hypothesis of mania. Fusaric acid administration was associated with a significant decrease in cerebrospinal fluid 3-methoxy-4-hydroxy-phenylglycol (the major metabolite of NE) and an increase in homovanillic acid (the major metabolite of dopamine), changes consistent with central DBH inhibition. Behavioral effects of fusaric acid appeared to depend on the preexisting clinical state. Patients with more severe mania, including evidence of preexisting psychotic features, became consistently worse (more psychotic), while patients with mild hypomanic symptoms showed no change or slight improvement. Conventional antimanic therapies, initiated after the fusaric acid protocol, were associated with improvement in the expected time period in all patients. 58 references. (Author abstract)

202785 Bruck, J.; Guss, H. Rehabilitationsheim der Caritas der Erzdiozese Wien, Obere Hauptstrasse 35, A-2326 Lanzendorf, Austria /**Aspects of neuroleptic depot therapy with special consideration of clinical experience with the peroral depot preparation Penfluridol (R-16-341 - Janssen).**/ Aspekte der neuroleptischen Depottherapie unter besonderer Berucksichtigung klinischer Erfahrungen mit dem peroralen Depotpraparat Penfluridol (R-16-341 - Janssen). International Pharmacopsychiatry (Basel). 9(3):152-165, 1974.

General clinicopharmacological, pharmacopsychiatric, psychological and social aspects of treatment with long-acting neuroleptics are discussed. Previous experiences have confirmed the importance of repository preparations for secondary prevention and their economic value. A report on an open clinical study of the long-acting agent Penfluridol (R-16-341 - Janssen), perorally administered to 50 patients suffering from schizophrenia is presented. The predominantly antipsychotic substance remains effective for 1 week after application of a single dose ranging from 20 to 120 mg. Apart from extrapyramidal side-effects, Penfluridol is well tolerated and no serious incidents were observed. (Author abstract modified)

203705 Vencovsky, Eugen; Loughrey-Grofova, Eva. Universitatsklinik Plzen (CSSR), Dukelska 69, Czechoslovakia /**Possible treatment of psychoneuroses with medazepam (Nobrium).**/ Uber die Moglichkeiten der Behandlung der Psychoneurosen mit Medazepam (Nobrium). Psychiatrie, Neurologie und medizinische Psychologie (Leipzig). 25(11):695-697, 1973.

Medazepam (Nobrium), a new benzodiazepine derivative, was administered to 50 patients, 21 of whom were suffering from a psychovegetative organic syndrome, 13 from a nervous phobic syndrome, 7 from an obsessive compulsive syndrome and nine with signs of masked depression. The therapeutic results were as follows: 34 patients (68%) experienced an improvement and only 16 patients (32%) did not show any improvement. The best results were obtained with the psychovegetative organic syndromes and nervous phobic syndromes. No important side-effects were observed and the laboratory tests were normal. (Journal abstract modified)

204372 Arnetoli, G.; Buyet, L. Clinica delle Malattie Nervose e Mentali, Universita di Firenze /**Treatment of Parkinson's disease by combining L-Dopa with a decarboxylase inhibitor.**/ Trattamento del morbo di Parkinson con associazione di L-Dopa e inibitore delle dopa-decabossilasi. Rivista di Patologia nervosa e mentale (Firenze). 94(1):29-55, 1973.

Forty-one patients with Parkinson's disease treated with levodopa combined with decarboxylase inhibitor (RO-4602) were studied analyzing age, etiology, severity, duration of syndrome, and period of treatment. Differences between L-Dopa treatment and L-Dopa combined with decarboxylase inhibitor were analyzed in relation to each individual symptom and to adverse reactions. The combination permits diminishing dosage from 5 to 10 times the normal dose of L-Dopa and produces a higher percentage of results (95.7%) as compared to L-Dopa alone (71.7%). There were no adverse reactions qualitatively different from those reported in the literature on L-Dopa treatment. There was a marked incidence of leukopenia, even if usually mild, and a remarkable reduction of cardiocirculatory and gastroenteric problems. The biological tolerability of the drug in moderate doses (525mg L-Dopa and 150mg of inhibitor) is good in most cases; thus these authors, in agreement with the literature, confirm that treatment with the combined L-Dopa and decarboxylase inhibitor is an important advance in the treatment of Parkinsonism. 45 references. (Journal abstract modified)

08 DRUG TRIALS IN SCHIZOPHRENIA

198075 Hogarty, Gerard E. Friends Medical Science Research Center, Inc., Baltimore, MD **NIMH-PRB collaborative outpatient schizophrenic study.** Psychopharmacology Bulletin. 10(2):54-55, 1974.

Two problems of contemporary psychiatry are studied: lowering the extremely high relapse rate of formerly hospitalized schizophrenics and exhancing the traditionally low level of adjustment and performance of schizophrenics while they

remain in the community. The effects of drug treatment with chlorpromazine and major role therapy (MRT--a combination of social casework and vocational rehabilitation) on recently discharged schziophrenics are considered. Data show that relapse rates on placebo are twice those on drugs; MRT also lowers relapse. However, the effect of MRT on placebo-treated patients does not differ from patients treated with placebo alone after 2 years. The specific contributions of both drug and sociotherapy in preventing relapse and promoting adjustment over time need to be identified. (Journal abstract modified)

198076 May, Philip R. A. University of California, Los Angeles, CA 90029 **Schizophrenia followup: a controlled treatment study.** Psychopharmacology Bulletin. 10(2):55, 1974.

The effectiveness of treating schizophrenics with drugs, electroconvulsive therapy and psychotherapy is systematically compared in a study of 228 first admission schizophrenics aged 16 to 45. The long-term effects of these methods are compared with the short-term results. Analysis of short-term data shows that drugs and drugs plus psychotherapy are the most effective and the least costly forms of treatment in terms of time and money. The long-term study is in the data analysis stage. (Journal abstract modified)

198094 Gershon, Samuel. New York University, New York, NY **Chlorpromazine metabolism in acute schizophrenia.** Psychopharmacology Bulletin. 10(2):65, 1974.

Methods for prediction of improvement in chlorpromazine (CPZ) treated schizophrenic patients are discussed, including radioisotopic procedures; fluorescent labeling of demethylated CPZ metabolites with fluorescein isothiocyanate; application of gas and liquid chromatography with flame ionization detection; preparation of 2,4-dinitrophenyl derivatives of CPZ metabolites; a scan technique for color complexes of CPZ by spectrophotometry; colorimetric assays for urine; and plasma-solvent extraction and deproteinization by ethanol or methanol for blood plasma. The scan technique provides the most practical and versatile assay of CPZ. (Journal abstract modified)

198098 Merlis, Sidney. Central Islip State Hospital, Central Islip, NY **Clinical chemical correlates of CPZ therapy.** Psychopharmacology Bulletin. 10(2):67, 1974.

The metablism of chlorpromazine (CPA) as reflected in urinary metabolites is analyzed. Chronic schizophrenics who have either improved or not improved on previous CPZ therapy, newly admitted schizophrenics, and normal individuals serve as subjects. Previously only 20% to 40% of orally administered CPZ could be traced in the urine. In this study, comprehensive biochemical analysis of urine and feces are made, and psychological tests (Gorham Proverbs and Raven Matrices) are administered. The objective is to discover the reason for occasional failure of chlorpromazine therapy. (Journal abstract modified)

198102 Payne, R. W. Temple University, Philadelphia, PA **Phenothiazine and schizophrenic thought disorder.** Psychopharmacology Bulletin. 10(2):69, 1974.

The hypothesis that reactive schizophrenics are benefited more by phenothiazines than process schizophrenics is being studied. The subjects are categorized into three groups, process schizophrenia, psychotic anxiety reaction, and overinclusive psychosis. Final assessment at the end of drug treatment is made to establish the responses to phenothiazine according to type of thought disorder. Tentative findings show that the three syndromes are independently definable disorders. Objectives are to refine the knowledge of schizophrenia and to improve methods for the clinical treatment of this disorder. (Journal abstract modified)

198103 Spohn, Herbert E. Menninger Foundation, Topeka, KS **Behavioral mechanisms of drug action in schizophrenia.** Psychopharmacology Bulletin. 10(2):69, 1974.

The changes that occur with antipsychotic drugs in the behavior of schizophrenics are studied. Subjects are withdrawn from all antipsychotic medication and half are given chlorpromazine, while others receive placebo. A variety of psychological performance measures are made during treatment. Objectives are to provide a better understanding of the effects of antipsychotic drugs on schizophrenics and to find new ways to predict these effects. (Journal abstract modified)

198104 Tokar, John T. Friends of Psychology Research, Inc., Baltimore, MD **The effects of thioridazine on language and thinking.** Psychopharmacology Bulletin. 10(2):69-70, 1974.

The effects of thioridazine on the language and cognition of acute schizophrenic patients are being studied. A reduction in the score of nonsense sentences used by the schizophrenics is noted. The "normal" belief system in the schizophrenics does not appear to be altered by drug treatment, but there are alterations in the aggression pattern of schizophrenics after 3 weeks of treatment. It is suggested that the drug effect is primarily that of filtering out nonsensical responses and a reduction in "scatter" or "splatter" type response. (Journal abstract modified)

198709 Yoshida, Masaki; Mori, Hirotoku; Kotorii, Ken. Department of Psychiatry, Kurume University School of Medicine, Japan **Clinical experience with clocapramine (Clofekton) for the treatment of schizophrenic patients.** Medical Consultation and New Remedies (Tokyo). 10(10):2423-2431, 1973.

The effect of clocapramine (Clofekton) on schizophrenia was studied, by treating 26 schizophrenic inpatients with this drug for periods from 4 weeks to 8 months. Treatment with clocapramine affected different subjects in different ways, but produced some alleviation of symptoms in over half of the patients tested. Positive effects included improved volition, spontaneity, communication, and other mental activities of the patients; these effects appeared 2 to 3 weeks after the beginning of treatment. Side-effects, such as akathisia, tremor, insomnia, and dry mouth were observed, but they disappeared after treatment with nitrazepam or reduction in the daily dose of clocapramine. 13 references.

198710 Watanabe, Manabu; Onodera, Isao; Miura, Keiichiro; Ishijima, Hiroshi; Kataoka, Noriaki; Miyagishi, Ben; Ito, Koichi; Kato, Takashi. Hokkaido University, Japan **Clinical experience with Forit: its activating effect on chronic schizophrenia.** Medical Consultation and New Remedies (Tokyo). 10(10):2415-2421, 1973.

The effect of Forit on chronic schizophrenia was studied, using as subjects 40 chronic schizophrenic inpatients with an average schizophrenic history of 12.6years. About half of the subjects responded favorably to Forit treatment. The drug was effective in increasing volition, activity, communication and facial expression. Side-effects included insomnia, Parkinsonism, vomiting, stomach ache, constipation, general fatigue and dry mouth. 8 references.

199625 Hogarty, Gerard E.; Goldberg, Solomon C.; Schooler, Nina R.; Ulrich, Richard F.; Collaborative Study Group. 3811 O'Hara St., Pittsburgh, PA 15261 **Drug and sociotherapy in the aftercare of schizophrenic patients: II. Two-year relapse rates.** Archives of General Psychiatry. 31(5):603-608, 1974.

The effects of maintenance chlorpromazine and major role therapy (MRT) in forestalling the relapse of 374 schizophrenic patients recently discharged from the hospital were studied. Chlorpromazine is significantly more effective than placebo in forestalling relapses. By 24 months, 80% of placebo treated patients have relapsed compared to 48% of those drug treated. Further, although drug therapy is more effective than placebo in both sexes, the size of the difference is significantly greater for women than men. There is no sex difference with placebo treatment. There is no significant effect of MRT during the entire treatment period. However, MRT does reduce relapses among those who survive in the community for 6 months after hospital discharge. These results were replicated at three clinics. 1 reference. (Author abstract)

199626 Hogarty, Gerard E.; Goldberg, Solomon C.; Schooler, Nina R.; Collaborative Study Group. 3811 O'Hara St., Pittsburgh, PA 15261 **Drug and sociotherapy in the aftercare of schizophrenic patients: III. Adjustment of nonrelapsed patients.** Archives of General Psychiatry. 31(5):609-618, 1974.

The effects of chlorpromazine and major role therapy (MRT) on the quality of community adjustment of schizophrenic patients during a 2-year period following hospital discharge were examined. Among patients in the community, those treated with combined drug and sociotherapy adjust better than those taking the drug alone; to a greater extent, those receiving placebo alone adjust better than those receiving placebo and sociotherapy. However, only 20% of those in the placebo group have not relapsed after 2 years while the comparable percentage for the drug group is 52%. Effects found on assessments made by psychiatrists, social workers, family ratings, and self-reports replicate at three clinics. Maximum restorative benefits require both maintenance phenothiazine and psychologic treatment continued beyond a single year following hospital discharge. 12 references. (Author abstract)

199993 Vandecasteele, A. J. A.; Vereecken, J. L. Th. M. Psychiatric Hospital "Sancta Maria", Langevelderlaan 1, Noordwijk, The Netherlands **A double-blind clinical evaluation of penfluridol (R-16-341) as a maintenance therapy in schizophrenia.** Acta Psychiatrica Scandinavica (Kobenhavn). 50(3):346-353, 1974.

Twenty-one female schizophrenics (age range 34-74 years) were included in a clinical study assessing the effectiveness of penfluridol as a basic maintenance therapy. The patients, all of whom had been successfully maintained on penfluridol for at least 6 months, were divided into two comparable groups. Group I (ten patients) received penfluridol and Group II (11 patients) received placebo under double-blind conditions for 6 months. When at any time during the study a patient deteriorated, haloperidol in individually adjusted doses was added to her treatment regimen. By the end of the study, eight of the 11 placebo patients received additional haloperidol, whereas only three of the penfluridol patients did. Evaluation of the scores on the rating scale showed no significant differences between the two treatment groups. The trial confirmed that penfluridol is a very suitable drug for the maintenance therapy of chronic schizophrenic patients. 15 references. (Author abstract modified)

200013 Zabrodin, G. D. no address /**The influence of reserpine on the serotonin metabolism in patients with schizophrenia and reactive conditions.**/ Osobennosti vliyaniya rezerpine na obmen serotonina u bol0nikh shizofreniey i s reaktivnimi sostoyaniyami. Zhurnal Nevropatologii Psikhiatrii Imeni S. S. Korsakov (Moskva). 74(8):1185-1191, 1974.

Peculiarities in the effects of reserpine in patients with schizophrenia and reactive conditions were studied. Reserpine was administered in doses of 2.5mg to 28 schizophrenics, 19 patients with reactive disorders, and 12 normals. Those with reactive conditions showed a somatovegetative reaction; normals showed a similar but milder reaction. After 3 hours there was an increase of serotonin (5-HT) in the blood and an increase of homovanillic acid (HVA) in the diurnal excretion. Schizophrenics rarely showed somatovegetative reactions. The level of 5-HT in the blood was initially high, but dropped after 3 hours; 5-HIAA excretion was insignificant. It was concluded that in schizophrenic patients there is a prevalence of bound 5-HT, while in patients with reactive conditions free forms prevail. 47 references. (Journal abstract modified)

200073 Stolyarov, G. V. no address /**The influence of neuroleptical drugs on catecholamine excretion.**/ Vliyanie neyroleptikov na ekskretsiyu katekholaminov. Zhurnal Nevropatologii i Psikhiatrii Imeri S. S. Kovsakova (Moskva). 74(7):1060-1064, 1974.

The effect of neuroleptic drugs on the excretion of adrenaline, noradrenaline, DOPA, and dopamine was studied. The subjects were 72 patients, most suffering from schizophrenia. No regular changes were found. The development of parkinsonism due to administration of phenothiazines was accompanied by a drop in dopamine excretion, but parkinsonism due to administration of haloperidol showed no such change. The dopamine noradrenaline coefficient decreased in parkinson symptoms, including those brought on by haloperidol, and again increased with their disappearance. 29 references. (Journal abstract)

200445 Masciocchi, A.; Reitano, S.; Vanini, M.; Cicchetti, V. Ospedale Psichiatrico Provinciale di Como, Italy /**Preliminary results of a controlled trial with sulpiride versus chlorimipramine in chronic schizophrenic patients with marked ideo-emotional poverty.**/ Risultati preliminari di una prova controllata con sulpiride versus clorimipramina in pazienti schizofrenici cronici con marcata sintomatologia deficitaria. Rivista di Patologia Nervosa e Mentale (Firenze). 95(1):47-52, 1974.

Preliminary results are reported of a controlled double-blind study with sulpiride versus chlorimipramine in chronic schizophrenic patients with marked ideo-emotional poverty. The therapeutic effects and tolerability of sulpiride and chlorimipramine are compared and data confirm that sulpiride and chlorimipramine are equally effective in improving the symptoms of ideo-emotional poverty and in altering the patients' behavior. 8 references. (Journal abstract modified)

200636 Morgan, Roger; Cheadle, John. Dept. of Psychiatry, St. Wulstan's Hospital, Malvern, Worchester, England **Maintenance treatment of chronic schizophrenia with neuroleptic drugs.** Acta Psychiatrica Scandinavica (Kobenhavn). 50(1):78-85, 1974.

The difficulties for the short-stay doctor of managing the drug treatment of long-stay schizophrenic patients are discussed and principles to follow are suggested. The results of following these principles 7 years are analyzed. Only 74 out

of a population of 475 chronic schizophrenics have been considered suitable for trial without drugs. Only five of these still remained off drugs. The relapses of the other 69 occurred after an average of about 4.5months. Possible reasons for the different results of drug withdrawal trials are suggested. 15 references. (Author abstract)

200803 Gerlach, Jes; Koppelhus, Per; Helweg, Eva; Monrad, Anette. St. Hans Hospital, Dept. E., DK-4000 Roskilde, Denmark **Clozapine and haloperidol in a single-blind crossover trial: therapeutic and biochemical aspects in the treatment of schizophrenia.** Acta Psychiatrica Scandinavica (Kobenhavn). 50(4):410-424, 1974.

Twenty male hospitalized schizophrenic patients participated in a single-blind crossover study of the antipsychotic properties, tolerance and side-effects of clozapine and haloperidol. It was found that both clozapine and haloperidol reduced the intensity of the core symptoms of schizophrenia. Clozapine, however, was significantly better than haloperidol for the treatment of somatic concern, anxiety, conceptual disorganization, tension and mannerism/posturing. In addition to its antipsychotic effect, clozapine had a pronounced sedative and hypnotic effect, particularly during the initial stages. Both drugs were well tolerated. Clozapine induced autonomic side-effects in the form of increased heartrate, orthostatic hypotension and hypersalivation. Haloperidol caused extrapyramidal side-effects. Determination of the homovanillic acid in the cerebrospinal fluid was carried out on five of the patients prior to and during treatment. These results suggest that haloperidol increases the turnover of brain dopamine to a greater degree than clozapine. The relations between the pharmacological biochemical data and the clinical observations are discussed. 24 references. (Author abstract modified)

200897 Menon, M. Sarada; Ramachandran, V.; Kasturirangan, V. Madras Medical College, Madras-3, India **A controlled clinical trial of pimozide (R 6238) -- a new neuroleptic.** Indian Journal of Psychiatry (Madurai). 15(4):325-328, 1973.

The efficacy of pimozide was compared with that of fluphenazine. Twenty male and 20 female chronic schizophrenics were randomly selected for study. Maintainance drugs were withdrawn and patients were observed for 6 weeks. Patients were then administered pimozide and fluphenazine for 8 weeks, and improvement was noted with both drugs. 5 references. (Author abstract modified)

200898 Ananth, J. V.; Nair, N. P. V. McGill University, Quebec, Canada **Niacin therapy in schizophrenia: a review.** Indian Journal of Psychiatry (Madurai). 15(4):329-340, 1973.

Treatment of schizophrenia with niacin (nicotinic acid) is reviewed. It is hypothesized that nicotinic acid, as a methyl acceptor, would reduce the methylated psychomimetic substances thought by some to induce schizophrenia. Niacin would also speed up tryptophan metabolism, inhibiting the formation of a certain indole derivatives that may induce schizophrenic symptoms. There is some evidence that a niacin deficiency is responsible for the psychotic symptoms of pellagra. Clinical studies are reported with adults and children which demonstrate its usefulness, but also point to the real and present danger of side-effects. 116 references.

201002 Weil-Malherbe, H. Division of Special Mental Health Research, NIMH, W. A. White Building, St. Elizabeths Hospital, Washington, DC 20032 **Serotonin and schizophrenia. (Unpublished paper).** Washington, D.C., NIMH, 108 p.

The roles of lysergic acid diethylamide (LSD) and serotonin in schizophrenia are examined. The mechanism of action of LSD is discussed. The search for an endogenous psychotogen with effects similar to those of LSD is reviewed; the most plausible candidates are methylated derivatives of tryptamine or serotonin which not only have hallucinogenic activity but also the potential of being synthesized by enzymes occurring in the body. No abnormality of serotonin synthesis or metabolism has been established in schizophrenia. Data on the behavioral effects of the amino acid precursors, L-tryptophan and L-5-hydroxytryptophan (5HTP), in schizophrenia are conflicting. Favorable results, in some cases, were recently reported when large doses of L-5HTP were given for several weeks. Evidence relating to a sleeping disorder in schizophrenics and its relationship to serotonin is briefly mentioned. 288 references. (Author abstract modified)

201669 Graz, B.; Crovato, E. Istituto Neuropsichiatrico Fatebenefratelli, Brescia, Italy **/Remarks on the use of flupentixol in treating chronic schizophrenia./** Rilievi sull0impiego del flupentixol nel trattamento di schizofrenici cronici. Riv. Sper. di Freniatria e Med. Legale delle Alienazione Ment. (Reggio). 98(1):175-189, 1974.

The results of 38 cases of chronic paranoid schizophrenia treated with flupentixol are reported. Positive results were obtained in 26% of the cases, concerning paranoids with atypical depression and minimal pathology. The drug apparently has a mobilizing property more than true incisive or antipsychotic properties as it had no effect on delirium and abnormal thought processes. The drug caused extrapyramidal effects in 34% of the cases and sleep disturbances in 26% of the cases. 12 references. (Author abstract modified)

201908 Avrutkiy, G. Ya.; Gurovich, I. Ya.; Zaytsev, S. G.; Ezhkov, A. A.; Magalif, A. Yu.; Prokudin, V. N. Moskovskii nauchno-issledovatel0skii institut psikhiatrii, Ministry of Health RSFSR, Moscow **/Some characteristics of pathology in schizophrenia during the two stages of psychopharmacological development./** Nekotorye kharakteristiki lekarstvennogo patomorfoza shizoffrenii na dvukh etapakh razvitiya psikhofarmakologii. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 74(9):1376-1384, 1974.

Case histories of schizophrenic patients admitted to mental hospitals in 1950, 1960, and 1970 were studied to determine the effects of changes in psychopharmacotherapy. Patients in the first group showed a statistically significant decrease in the frequency of expression and an increase in the reversibility of the main psychopathological disorders with the exception of depressive conditions. Patients in the second group showed favorable changes in depressive states, a more frequent encapsulation of delusions, and an improvement in the quality of remissions. These changes reflect stages in the development of psychopharmacotherapy. 51 references. (Journal abstract modified)

201910 Almazov, B. N. Sverdlovskii meditsinskii institut, Sverdlovsk, USSR **/Comparative results of a pharmacological loading with aminazine and haloperidol in schizophrenic patients./** Sravnitel0nye rezul0taty farmakologicheskoy nagruzki aminazinom i galoperidolom pri lechenii bol0nykh prostoy formoy shizofrenii (po dannym bolevoy sensografii). Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 74(9):1397-1401, 1974.

The influence of pharmacological loading with aminazine and haloperidol on the effective component of pain reaction in schizophrenic patients was studied. Pain sensography was used

to register patients' reactions. In most cases aminazine and haloperidol removed the hypoalgesia present in some cases of schizophrenia and restored emotional reactions to pain. In other cases aminazine did not affect the character of reaction to pain and haloperidol increased the reaction, but only during the period of neuroleptic activity. 10 references. (Journal abstract modified)

202603 Shimizu, Hidetoshi. Zentsuji National Hospital, Kagawa, Japan **Clinical trial of flupentixol in patients with chronic schizophrenia: especially in patients having difficulty in rehabilitation owing to decreased expression, apathy and disturbance of rapport.** Iryo (Therapeutics) (Tokyo). 28(5):372-378, 1974.

A clinical trial of flupentixol is reported in patients with chronic schizophrenia. The drug was given to 21 subjects for 5 to 210 days in combination with antiparkinsonian drugs. The schizophrenic symptoms were well improved in four cases, moderately improved in three, temporarily improved in eight, unchanged in three and worsened in three. The drug showed effect in 71% of patients with affectional disturbances and in 52% of the patients with volitional disturbances. The following side-effects were noted: sleep disturbances, bursts of psychic symptoms, and increased libido. Hypotension, Parkinson's syndrome dullness, nausea and anorexia were also observed. Side-effects disappeared after cessation of treatment or on discontinuation of the drug. The drug is seen to be effective against the fundamental symptoms of schizophrenia. 6 references. (Journal abstract modified)

202693 Breakey, William R.; Goodell, Helen; Lorenz, Patrick C.; McHugh, Paul R. Christian Medical College, Ludhiana, Punjab, India **Hallucinogenic drugs as precipitants of schizophrenia.** Psychological Medicine (London). 4(3):255-261, 1974.

The drug taking histories of 46 schizophrenics and 46 matched controls were examined. Schizophrenics on average used a wider variety of drugs, in greater amounts. Schizophrenics who had used drugs experienced the onset of symptoms on average 4 years earlier than nonusers and were also admitted to hospital 4 years earlier, on average. Those schizophrenics who had used drugs had had better premorbid personalities than the nondrug users. These results are indicative of some precipitating role of drug abuse in the onset of schizophrenia. 14 references. (Author abstract)

202787 Ban, Thomas A. Division of Psychopharmacology, McGill University, Montreal, Quebec, Canada **Negative findings with nicotinic acid in the treatment of schizophrenias.** International Pharmacopsychiatry (Basel). 9(3):172-187, 1974.

In view of the controversy regarding the effectiveness of nicotinic acid therapy in schizophrenic patients, a series of systematic studies were designed to obtain relevant information on this treatment. Since the initiation of these collaborative studies, five of the 12 originally designed clinical trials have been completed. Findings suggest that the administration of nicotinic acid in the dosage of 3000mg/day has no therapeutic effect; or may even have a negative therapeutic effect, in unselected groups of schizophrenic patients. 47 references. (Author abstract)

202879 Gardos, George. Boston State Hospital, 591 Morton St., Boston, MA 02124 **Are antipsychotic drugs interchangeable?** Journal of Nervous and Mental Disease. 159(5):343-348, 1974.

The interchangeability of effective antipsychotic compounds was investigated in a clinical setting. Sixty formerly hospitalized chronic schizophrenics were randomly assigned to chlorpromazine, thiothixene, or continued doctor's choice medication groups. Dose of antipsychotic medication and schedule of administration were kept constant. During the 2 year study period 16 patients (44%) in the combined chlorpromazine and thiothixene groups ("switched group") underwent clinical deterioration to an extent that they had to be terminated from the study. Only two patients (12%) of the control group relapsed during the same period. The significant difference in relapse rates is attributed to the change in antipsychotic medication. Relapses were equal in number during the first and second 6 months of the study. The new antipsychotic (chlorpromazine or thiothixene) may have delayed, but did not prevent, the relapse of these patients. The study findings show that for individual schizophrenic patients antipsychotic drugs are not interchangeable. The clinician should be wary of switching drugs in a stabilized chronic schizophrenic, since relapse may be precipitated by the medication change. 14 references. (Author abstract)

203213 Eisenberg, Leon. Department of Psychiatry, Harvard University Medical School, Boston, MA **The pace of progress.** World Health. October: p. 4-7, 1974.

Developments in genetics and biochemistry in treating mental illness are reported. Schizophrenia is concentrated in biological families and occurs at no more than the average rate of the population among adoptive families. The patient inherits a susceptibility to schizophrenia, but the action of some as yet unknown environmental precipitant is required for the disease to manifest itself. It is revealed that tricyclics affect the action of norepinephrine in the brain by interfering with its reabsorption and inactivation. Evidence suggests that norepinephrine is related to mood, insufficient amounts leading to depression and excess resulting in mania. The phenothiazines which improve schizophrenia block the effects of dopamine on its receptors; amphetamines, drugs that can produce a toxic state resembling schizophrenia, enhance dopamine action.

203666 Beier, Rolf; Vehreschild, Torsten. Universitats-Nervenklinik, DDR-25 Rostock 9, Germany /**Aponeuron treatment of chronic schizophrenics with reduced drive.**/ Uber die Behandlung von antriebsgeminderten chronischen Schizophrenien mit Aponeuron. Psychiatrie, Neurologie und medizinische Psychologie (Leipzig). 25(6):375-379, 1973.

Twenty-three chronic schizophrenics, with signs of a severe reduction in drive were given a daily dose 50-80mg Aponeuron for 1-10 months. All patients showed an improvement in their drive which also benefited other psychic performances. Neither euphoric addictive effects nor an exacerbation of psychosis were apparent. Opposite results were obtained when higher doses of aponeuron were administered to patients with severely defective syndromes, suicide prone patients and those with a tendency to aggression and affective control weakness. 13 references. (Journal abstract)

204169 St. Laurent, Jacques; Carle, Roger; Dumais, Bernard; Domingue, D. Department of Pharmacology, Faculty of Medicine, University of Ottawa, Ontario, Canada **Monthly intermittent chemotherapy of chronic schizophrenic outpatients with pipothiazine palmitate.** Canadian Psychiatric Association Journal (Ottawa). 19(6):583-591, 1974.

A long-term open study of a new sustained action neuroleptic was undertaken in 23 chronic schizophrenic outpatients. Pipothiazine palmitate (R.P. 19,522) was administered by in-

tramuscular injection at an average dose of 100mg every 4 weeks. Psychiatric assessment revealed that the drug provided good control of psychotic symptomatology, and there were indications that patients responded better to the test medication than they did to their standard oral antipsychotic maintenance therapy. Extensive laboratory and functional tests demonstrated that the drug is well tolerated. Side-effects were generally not serious and included primarily somnolence, tremor, akathisia, and blurring of vision. Since the drug demonstrated its capacity to control psychotic symptoms with low dosages over an extended period of time, it is suggested that double-blind study comparing this drug with other neuroleptics is warranted. Pipothiazine palmitate may be an efficient form of maintenance therapy for ambulatory patients. 14 references. (Author abstract modified)

204415 Eckmann, F.; Gebert, Alfred; Lienert, G. A. no address /**Differential effects of neuroleptic drugs in chronic schizophrenics: a configuration analytical evolution.**/ Differentielle Wirkung von Neuroleptika bei chronisch Schizophrenen: eine konfigurationsanalytische Auswertung. Arzneimittel-Forschung (Aulendorf). 24(8):1135-1138, 1974.

A sample of 502 patients diagnosed as chronic schizophrenics was treated with or without neuroleptics. Treatment was defined as successful if a recovered patient was definitively discharged and not readmitted to the hospital within 7 years. For evaluating therapeutic effects differentially, the patients were subdivided as productive or unproductive schizophrenics according the Haase's schedule and as having or not having social contacts with family members. Configural frequency analysis showed that neuroleptic treatment is mostly effective when applied to unproductive schizophrenics having social contacts. These and other differential therapeutic effects are discussed clinically and methodologically. 7 references. (Journal abstract modified)

204430 Koga, Itsuyuki. Department of Neuropsychiatry, Tottori University, School of Medicine, Japan **A polygraphic study of tolerance of schizophrenics to chlorpromazine.** Journal of the Yonago Medical Association (Yonago). 25(2):122-138, 1974.

Occurrences of the sleep EEG (percent time waking EEG) and of the galvanic skin reflex (GSR) were studied polygraphically in 22 schizophrenics and 10 normal control subjects to investigate the neurophysiologic tolerance of schizophrenics to chlorpromazine (CPZ). Findings indicate: 1) the average percent waking EEG in schizophrenics at rest before CPZ administration was significantly higher than that of normals; 2) after CPZ administration, schizophrenics did not show any significant difference between premedication and postmedication, while a significant decrease from the premedication value was found in normals; 3) CPZ medication presented no significant decrease in the incidence of spontaneous GSR in schizophrenics from the premedication value, but normals exhibited significantly lower values. It is concluded that the oral CPZ polygraphy is useful in investigating tolerance in psychotic patients. Pathophysiology of schizophrenics is discussed from the standpoint of elevated activity level in the central nervous system. 41 references. (Author abstract modified)

204852 Bowers, Malcolm B., Jr. Yale University School of Medicine, New Haven, CT 06520 **Thioridazine: central dopamine turnover and clinical effects of antipsychotic drugs.** Clinical Pharmacology and Therapeutics. 17(1):73-78, 1975.

Thioridazine was administered to 14 patients diagnosed as within the "schizophrenic spectrum" with the result that substantial improvement in psychotic symptoms was achieved while significant extrapyramidal side-effects (EPS) occurred in only one patient. Under these conditions lumbar cerebrospinal fluid homovanillic acid following probenecide was significantly elevated. Cerebrospinal fluid probenecid and 5-hydroxyindoleactic acid declined significantly during treatment with thioridazine. Taken in conjunction with the results of other studies, it appears that cerebrospinal fluid homovanillic acid can be moderately elevated in man during successful treatment with antipsychotic drugs when EPS are virtually absent. Possible interpretations of these results are discussed with regard to the clinical effects of antipsychotic drugs as they relate to central dopaminergic activity. 32 references. (Author abstract)

205179 Oh, Min-Woong. Dept. of Neuropsychiatry, Catholic Medical College, Seoul, Korea **Schneiderian first rank symptoms and clinical features of schizophrenia.** Journal of Catholic Medical College (Seoul). 26:831-837, 1974.

The relationship between Schneiderian criteria of schizophrenia and clinical features of schizophrenia, number of admissions, neuroleptic dosage level, use of electroconvulsive treatment and prognosis, was investigated in a study of 140 schizophrenic patients. The results indicate: no significant relationship between Schneiderian first rank symptoms and age, sex or marital status; patients with Schneiderian first rank symptoms were 60% of all the patients and 74% of the readmissions; patients with Schneiderian first rank symptoms received larger doses of neuroleptics, more had electroconvulsive treatment and poor prognosis than those without Schneiderian symptoms; and the most frequent Schneiderian first rank symptom was the experience of influence. 13 references. (Journal abstract)

205448 Etevenon, P.; Peron-Magnan, P.; Rioux, P.; Littre, M. F. Paris, France **EEG statistical spectral analysis of schizophrenic patients.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):700, 1973.

A paper presented at the 8th International Congress of Electroencephalography and Clinical Neurophysiology reported a study in which electroencephalogram (EEG) tracings of seven schizophrenic patients were recorded on a polygraph and magnetic tape and sequentially analyzed by EEG statistical spectral analysis. After a period of washout of at least 15 days, 1 hour control records were registered each week during 2 weeks and then thioridazine was administered. Two other records were obtained after 4 and 14 days of treatment. Clinical examination was in agreement with EEG classification, distinguishing one chronic delusional psychosis, four hebephrenic patients and two paranoid schizophrenics. Each patient presented a characteristic statistical spectral pattern. When compared to the first control record, a shift towards higher mean frequencies and slight increase in mean amplitude values were generally observed after 24 days of treatment. When comparing analysis of the first control and after 14 days of treatment, lateralization changes were observed in the alpha band, mostly in three patients, between left and right parieto-occipital leads. (Author abstract modified)

205581 Taussigova, D.; Vinar, O.; Bastecky, J. Prague 1, Benediktska 9, Czechoslovakia **Oxyprothepine in schizophrenia.** Activitas Nervosa Superior (Praha). 16(3):163-165, 1974.

At the 16th Annual Psychopharmacological Meeting, a study of the use of oxyprothepine in schizophrenia was presented. A favorable therapeutic response was observed more frequently in patients with lower doses. This finding might be attributed to the policy to increase the doses in patients who did not im-

prove on low doses. As a rule, these patients tolerated high doses without serious side-effects. These findings were explained by the hypothesis that the treatment failures were due to a poor resorption (there is a thorough control that the patients ingest the drugs in the wards) and/or some kind of resistance on sites of the drug effect. The frequency and intensity of side-effects was comparable to their frequency and intensity observed with other potent incisive neuroleptic drugs. 11 references.

205582 Svestka, J.; Nahunek, K.; Rodova, A.; Ceskova, E. Psychiatric Clinic Brno-Bohunice, Jihlavska 102, Czechoslovakia **A controlled comparison of oxypertine and perphenazine in schizophrenic psychoses.** Activitas Nervosa Superior (Praha). 16(3):165-166, 1974.

At the 16th Annual Psychopharmacological Meeting, a double blind and crossover study of oxypertine with perphenazine in 22 men and 22 women, hospitalized in a closed ward in the psychiatric clinic, was reported. Both piperazine derivatives proved their antipsychotic efficacy in about 75% of patients. In the group of 44 schizophrenic patients studied, 38% displayed a certain individually different therapeutic effect of one or the other compound. 3 references.

205584 Faltus, F. Psychiatric Clinic, Praha 2, Ke Karlovu II, Czechoslovakia **The depot compounds Moditen (fluphenazine) and IMAP (fluspirilene) in clinical practice.** Activitas Nervosa Superior (Praha). 16(3):167-168, 1974.

At the 16th Annual Psychopharmacological Meeting, a study in which the therapeutic effect was compared in two groups of schizophrenic patients treated with depot injection preparates Moditen (fluphenazine) and IMAP was reported. Of the 29 (fluspirilene) patients treated with Moditen, 27 were evaluated; of these, in 23 (85.1%) remission was maintained well. Of the 17 IMAP treated patients 16 were evaluated. The frequency and intensity of psychotic symptoms were assessed at the beginning of maintenance treatment and their improvement in the course of one year. The effect of Moditen on florid psychotic symptoms (hallucination, delusions, thought disturbances) appears to be somewhat better than that of IMAP; the difference is not significant. IMAP had a distinctly better effect on sociability and affectivity.

205585 Niturad, A.; Ciurezu, T.; Cucu, I. Clinic of Psychiatry, Bucarest, Rumania **Maintenance treatment of schizophrenia with long-acting fluphenazine.** Activitas Nervosa Superior (Praha). 16(3):167, 1974.

At the 16th Annual Psychopharmacological Meeting, a study in which the efficacy of long-acting fluphenazine (enanthate and decanoate) for maintaining the remission of schizophrenia was compared with the classical methods using other neuroleptics was reported. Two groups of 30 female outpatients, schizophrenics in the remission phase, matched for age, clinical form, duration of the disease, duration of the observation and residual symptoms were treated either with fluphenazine or with other neuroleptics: thioproperazine, trifluoro-methylpiperazine, levopromazine and chlorpromazine. The fluphenazine group displayed superior improvement in a greater proportion of patients and a significantly restored working ability. In no case was it necessary to interrupt the neuroleptic treatment because of intolerance or side-effects. The side-effects were of medium or mild intensity and were alleviated with antiparkinsonian medication.

205591 Rodova, A.; Nahunek, K.; Svestka, J. Psychiatric Clinic, UJEP Brno Bohunice, Jihlavska 102, Czechoslovakia **An attempt to classify neuroleptic drugs on the basis of short-term clinical comparative studies.** Activitas Nervosa Superior (Praha). 16(3):169-170, 1974.

In a paper presented at the 16th Annual Psychopharmacological Meeting, the results of short-term controlled crossover studies in schizophrenic patients were used for comparing the effectiveness of 13 neuroleptic drugs. Perphenazine was selected as the central drug of comparison, and its effect was compared interindividually and intraindividually. Octoclothepin, oxyprothepin and clothiapin form a group having a greater affinity to the extrapyramidal as well as autonomic system and a marked hypnotic component. Another cluster is formed by thioridazine, levopromazine and clozapine with a markedly predominant sedative autonomic symptomatology, of which clozapine had the lowest affinity to the extrapyramidal system. Another cluster in the arrangement is formed by neuroleptics in which the sedative autonomic and extrapyramidal profile was close to that of perphenazine. Butyrophenone, methylperidol and trifluperidol showed a lower affinity to the autonomic system and a little higher affinity to the extrapyramidal system. 3 references.

205592 Pislova, J.; Pisl, I.; Petranova, T.; Petrova, M. Mental Hospital, Dobrany u Plzne, Czechoslovakia **Clinical experience with carpipramine (Defekton).** Activitas Nervosa Superior (Praha). 16(3):168-169, 1974.

At the 16th Annual Psychopharmacological Meeting, a clinical trial in which carpipramine was administered to 15 female schizophrenic patients aged 19-63 was reported. The generally most prominent changes of the rating scale were in the items of aggressivity, motor activity, affectivity, sociability and speech. The changes of other items were slight only. The patient with chronic psychasthenia showed excellent improvement and was discharged from the hospital.

09 DRUG TRIALS IN AFFECTIVE DISORDERS

198080 DiMascio, Alberto. Tufts University, Boston, MA **NIMH-VA lithium collaborative study.** Psychopharmacology Bulletin. 10(2):57-58, 1974.

Lithium's effectiveness in reducing manic symptoms during an acute episode, and in preventing recurrence of manic and depressive states is evaluated. Persons with manic or depressive illnesses and those diagnosed as schizoaffective are subjects. Lithium carbonate was effective in treating the manic phase of manic-depressive psychosis, but in schizoaffective, manic phase patients, lithium increased agitation and schizoid behavior. These symptoms diminished rapidly when lithium treatment was terminated. (Journal abstract modified)

198084 Smith, Kathleen. Washington University, St. Louis, MO **Drug therapy in depression.** Psychopharmacology Bulletin. 10(2):60, 1974.

The effects of imipramine (Tofranil), procyclidine, chlorpromazine (Thorazine), and lithium carbonate were studied in different types of depressed patients. Side-effects are listed for the chlorpromazine-imipramine study, and it is suggested that the dosage of chlorpromazine used (1200mg/kg) was too high. Other findings in the imipramine-chlorpromazine study include the following: a) imipramine is effective in treating psychotic depressives, by improving motor retardation and stimulating interest and involvement in activities; and chlorpromazine has an opposite effect; b) neurotic depressives do equally well on either drug or on placebo; c) chlorpromazine is more effective in reducing symptoms of guilt worthlessness,

hostility, anxiety, and bizarre thought and behavior. (Journal abstract modified)

198229 van Praag, Herman M.; van den Burg, Willem; Bos, Erik R. H.; Dols, Louise C. W. Department of Biological Psychiatry, Psychiatric University Clinic, Groningen, the Netherlands **5-Hydroxytryptophan in combination with clomipramine in "therapy-resistant" depressions.** Psychopharmacologia (Berlin). 38(3):267-269, 1974.

In some depressive patients, regarded as therapy resistant, the antidepressive effect of 1-5-hydroxytryptophan (in combination with a peripheral decarboxylase inhibitor) was enhanced by clomipramine at a dosage which, as such, was suboptimal. It is concluded that the therapeutic effect of 1-5-hydroxytryptophan is based on increase of serotonin at central serotonin receptors. 7 references. (Author abstract)

199212 Ose, Eivind. Psychiatrisches Institut, Neevengaarden Krankenhaus, Universitat zu Bergen, N-5000 Bergen, Norway **/Depression treated with chlorimipramine with special analysis of change in blood pressure by infusion./** Chlorimipramin-Behanddlung von depressiven Kranken mit spezieller Analyse der Blutdruckanderungen bei Infusionen. Arzneimittel-Forschung (Aulendorf). 23(6):817-823, 1973.

The effects of chlorimipramine on various depressive conditions, and the potentiation of these effects through administration by infusion were studied. Chlorimipramine was initially given as an infusion to 61 patients; 60 females and one male. To 13 patients chlorimipramine was administered in tablet form throughout the trial. The therapeutic results were shown to be best in the treatment of endogenous depressions. There was a tendency for the results in the older age groups to be inferior. The frequency and type of side-effects were the same as those found in treatment with imipramine. In the beginning of the trial chlorimipramine infused in 1000 ml fluid in each infusion was given, and in some cases a rise in blood pressure in connection with these infusions was observed. The conclusion is that there is a speedier effect when chlorimipramine is administered by infusion compared with other tricyclic antidepressives administered orally. 40 references. (Author abstract modified)

199631 Murphy, Dennis L.; Beigel, Allen. Laboratory of Clinical Science, NIMH, NIH Clinical Center, 10-3S229, Bethesda, MD 20014 **Depression, elation, and lithium carbonate responses in manic patient subgroups.** Archives of General Psychiatry. 31(5):643-648, 1974.

Depressive elements were observed on a quantitative behavioral rating scale during manic episodes in 28 of 30 patients, suggesting that most manic patients manifest a "mixed" manic-depressive picture. A factor analysis of the scale confirmed a "core" group of manic symptoms as well as a dichotomous grouping of elated grandiose (E-G) and paranoid destructive (P-D) patients. It also suggested a close relationship between the presence of rated depression during mania and the particular symptomatic complex found in the P-D subgroup of manic patients. Elation ratings were not significantly correlated with total mania scale ratings in all, but only in the subgroup of E-G patients. These differences had apparent relationships to therapeutic responses to lithium carbonate; manic patients in the E-G subgroup responded more frequently than did patients in the P-D subgroup. 22 references. (Author abstract)

200072 Smulevich, A. B.; Zavidovskaya, G. I.; Igonin, A. L. Institute of Psychiatry, Academy of Medical Sciences, Moscow **/Problems of clinical effectiveness and use of lithium salts in psychiatric practice./** Voprosi klinicheskoy effektivnosti i metodiki primeneniya soley litiya v psikhiatricheskoy praktike. Zhurnal Nevropatologii i Psikhiatrii Imeni S. S. Korsakova (Moskva). 74(7):1052-1060, 1974.

The effectiveness of treating affective attacks with lithium salts is studied. The experiment involved 100 hospitalized patients and a control group of 100 also in the hospital. In cases of schizophrenia, lithium salts appeared to be effective only where there was a tendency towards stabilization, and especially when the affective disorders had no connection with the constitutional features but were more of a neteronomous disturbance. In cases of manic-depressive psychosis, lithium salts were the most effective when the disease was in the intermittent phases with a clear cut periodicity. Unfavorable results were obtained in cases where there were signs of a progressive development of the psychosis. 24 references. (Journal abstract modified)

200103 Zakharova, N. N. no address **/A correlation between the influence of psychotropic drugs and emotional stress./** O vliyanii psikhotropnikh sredstv pri emotsional0nom stresse. Zhurnal Nevropatologii i Psikhiatrii Imeni S. S. Korsakova (Moskva). 74(2):277-282, 1974.

The tranquilizing effect of psychotropic drugs with different mechanisms of alleviating emotional stress was studied. Changed perception in conditions of negative emotions of patients with psychopathic posttrauma syndrome was studied. Relative effectiveness of the drugs, in descending order, was amisil, aminasine, seduxen, melipramin. Some of the drugs had a more selective tranquilizing action, others combined tranquilizing effect with stimulation or inhibition of the CNS. 17 references. (Journal abstract modified)

200237 Behavioral Sciences Tape Library, c/o Sigma Information, Inc., 240 Grand Avenue, Leonia, NJ 07601 (201-947-4154) BST (S)$7.95 ea. **Psychopharmacologic Treatment of Affective Disorders.** AT 1 7/8 IPS cassette 60 min ea., 1974.

Current concepts of psychopharmacology are presented as the basis for a clinically oriented discussion of agents useful in depression and mania. Particular emphasis is placed on the use of lithium. Stress is on the solution of practical problems in the management of affective disorders with the aid of psychopharmacologic agents. The lecturer is Dr. Baron Shopsin of the New York University School of Medicine. The individual tape titles are: 1) Psychopharmacology of depression; 2) Psychopharmacology of Mania; 3) Use of lithium in psychiatry; and 4) Use of lithium in psychiatry (cont.)

200481 Jones, Granville L. Fair Oaks Hospital, Summit, NJ **Observations on the treatment of depressions.** Journal of the Medical Society of New Jersey. 71(10):769-771, 1974.

Two hundred consecutive hospital admissions over a 10-month period for affective disorders as well as other depressions were studied initially and then reviewed after 5 years in order to determine the relationship between the types and dosages of medical treatments and the rate of recidivism. Of the 200 patients, 160 received convulsive shock treatments, most of them combined with drugs. The patients receiving six or fewer shocks showed a higher return rate than those receiving eight or more shocks. The 31 patients receiving drugs only had a higher return rate. Patients staying longer than the average length of hospitalization had a substantially lower readmission rate. Therefore, convulsive shock treatment of depressive conditions seems to be more effective when eight

or more treatments and a somewhat longer hospitalization are employed in treatment.

200568 Schou, M. Statshospitalet, 8240 Risskov, Denmark **/The current status of lithium recidivism prophylaxis in endogenous affective illnesses./** Heutiger Stand der Lithium-Rezidivprophylaxe bei endogenen affektiven Erkrankungen. Nervenarzt (Berlin). 45(8):397-418, 1974.

Double-blind studies of two groups, and open studies of one patient group have shown long-term lithium treatment effective in reduction or prevention of recurrent endogenous affective psychoses, whether bipolar or monopolar, but less effective in residual schizoid affective disturbances. Clinically, lithium presents problems regarding treatment initiation, duration, and psychosocial problems after treatment. Side-effects can be controlled by: a) distribution of daily doses into many small doses; and b) administration of a slow release tablet, or small morning dose, followed by a larger night time dose. A receptor blocker, like propranol, can reduce hand tremors induced by lithium. Other precautions against thirst, excessive urination, administration during pregnancy or nursing, and lithium intoxication, are discussed. 105 references.

200581 Ball, J. R. B.; Grounds, A. D. Private Bag 8, Post Office, Parkville, Vic. 3052 **Head injury, hypopituitarism and paranoid psychosis: circumcision for the "Singapore virus."** Medical Journal of Australia (Sydney) 2(11):403-405, 1974.

A case of paranoid psychosis associated with hypopituitarism is reported. The patient was admitted to a psychiatric hospital in a highly delusional state and found to be suffering from hypopituitarism. The patient's medical history also indicated two instances of concussion due to motorcycle accidents. Treatment with prednisolone and thyroxine aggravated the psychiatric condition, necessitating electroconvulsive shock therapy. The patient rapidly improved and subsequent relapse responded well to trifluoperazine. Methyltestosterone was added to the patient's endocrine therapy and within 5 months of his admission, the patient was discharged symptom-free. 7 references.

200584 Greenblatt, David J.; Shader, Richard I. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **Rational use of psychotropic drugs: IV. antidepressants.** Journal of the Maine Medical Association. 65(11):283-288, 1974.

The rational use of antidepressants is discussed. The clinical response to antidepressant drugs depends strongly upon the category of depression being treated. Tricyclics and monoamine oxidase (MAO) inhibitors are the two major categories of clinically useful drugs. All tricyclic drugs must be given in adequate dosage, which usually means reaching a daily dose of 150mg per day of imipramine or its equivalent. Tricyclic antidepressants exert important clinical effects on mood only after a significant lag period. All tricyclic antidepressants have significant atropine-like effects. Clinically important cardiac toxicity probably can occur with therapeutic doses. Potential drug interactions are surveyed. Although more hazardous and more expensive, electroconvulsive (ECT) therapy is more consistently effective. Patients with disabling depression who fail to respond to tricyclic antidepressants should be considered as candidates for ECT. 99 references.

200922 Satija, D. C.; Advani, G. B.; Bansa, A. N. Department of Psychiatry, Jawaharlal Nehru Medical College, Ajmer, Rajasthan, India **A double blind clinical trial of new antidepressant, Surmontil.** Indian Journal of Psychiatry (Madurai). 15(4):341-346, 1973.

A double-blind clinical trial of Surmontil (trimipramine) and imipramine in depressive states is reported. Both drugs were given 75-150mg/day for 6 weeks. After completion of the trial 80% of the cases improved or recovered with trimipramine, and 70% cases with impramine. Other effects of both medications are mentioned, including side-effects. 1 references. (Author abstract modified)

201000 Baron, Miron; Gershon, Elliot S.; Rudy, Victor; Jonas, Wulff Z.; Buchsbaum, Monte. Dept. of Research, Jerusalem Mental Health Center, Ezrath Nashim, Jerusalem, Israel **Lithium response in depression as predicted by unipolar/bipolar illness, average evoked response, catechol-O-methyl transferase and family history. (Unpublished paper).** Bethesda, Maryland, NIMH, 26 p.

The antidepressant efficacy of lithium carbonates was assessed in a double-blind trial in 23 hospitalized depressed patients. Unequivocal response was significantly more frequent in bipolar than in unipolar depressed patients. Lithium responders had a greater visual average evoked response amplitude increase in response to increased stimulus intensity, termed "augmenting". No correlation could be demonstrated between lithium efficacy and either erythrocyte catechol-O-methyl transferase activity, age of symptom onset, number of hospitalizations, or family history of affective disorders. 46 references. (Author abstract)

201513 Berg, Ian; Hullin, Roy; Allsopp, Michael; O'Brien, Patrick; MacDonald, Robert. Dept. of Psychiatry, University of Leeds, Leeds, England **Bipolar manic-depressive psychosis in early adolescence: a case report.** British Journal of Psychiatry (London). 125:416-417, 1974.

A case history is reported of an adolescent girl who had bipolar manic-depressive psychosis starting at 14 years of age. Symptoms at the time of onset included severe anorexia, school phobia and attempted suicide. The patient required unusually high doses of lithium carbonate to obtain adequate plasma levels, and there was a tendency for the administration of antidepressant medication to cause her to switch rapidly from depression to hypomania. The last two findings were shared by her father who also had bipolar manic-depressive psychosis. 6 references.

201655 Ito, Ryuta; Tsutsui, Sueharu. School of Medicine, Toho University, Omori, Tokyo, Japan **Treatment of masked depression.** Journal of the Medical Society of Toho University (Tokyo). 19(6):565-574, 1972.

The methods of diagnosing masked depression (MD) through physical and mental functional symptoms and methods of its treatment and problems are cited. Masked depression is most frequently found in the middle-aged women. Its symptoms may manifest physically: insomnia, fatigue, poor appetite, muscle and bone aches; these symptoms are often misdiagnosed as other ailments. The patient's personality, changes in daily body function, weight, and sleep pattern are points to watch and examine. The most commonly used drugs to treat MD are imipramine (Tofranil) and amitriptyline (Tryptanol). Doxepin is also used, especially in the U.S. Frequently, neuroleptic and hypnotic drugs are used to treat insomnia in MD. Included also are some guidelines for the use of therapeutic drugs, dangers, and side-effects, as well as one case report and an interview with Dr. Tsutsui. 5 references.

201667 Vescovini, L. Istituti Neuropsichiatrici S. Lazzaro, Reggio Emilia, Italy **/Clinical double-blind study on the activity of a new antidepressant: caroxazone (F.I. 6654)./** Studio clinico

"double blind" sull'attivita di un nuovo composto antidepressivo: il caroxazone (F.I. 6654). Riv. Sper. di Freniatria e Med. Legale delle Alienazione Ment. (Reggio). 98(1):151-165, 1974.

Clinical results showed that a new drug, caroxazone, has an antidepressive effect similar to that of imipramine. The drug's most distinct therapeutic effects included: a dynamic and disinhibiting effect on psychomotor actions with reduction of sense of insufficiency and incapacity; reduction and abolition of feelings of sadness and the idea of incurability; a beneficient effect on paranoid symptoms. Other manifestations of depression were influenced with the exception of insomnia. Side-effects were negligible. 7 references.

201668 Seminara, Benedetto. Ospedale Psichiatrico Provinicia Autonoma di Trento, Pergine, Italy /**A case of severe headache as an equivalent of affective disorder.**/ Un caso di equivalente cefalgico di distimia. Riv. Sper. di Freniatria e Med. Legale delle Alienazione Men. (Reggio). 98(1):166-174, 1974.

The literature on depressive syndromes is briefly reviewed, and a typical case of severe headache with an affective disorder is discussed. Fundamental clinical characteristics which aid in diagnosing depressive syndromes include: biographical data, which often reveals depressive syndromes in the patient's past which are clinically analogous or different from the present syndrome; episodic development; the vague clinical appearence of a "classic" depressive state; the evolution toward a more clearly depressive framework; and the ex adjuvantibus criterion. The case cited was difficult to diagnose, as the only symptom was the occurrence of severe headaches. The patient was treated with imipramine and amitriptyline. 24 references.

202248 Bowers, Malcolm B., Jr. Dept. of Psychiatry, Yale University School of Medicine, 33 Cedar St., New Haven, CT 06510 **Lumbar CSF 5-hydroxyindoleacetic acid and homovanillic acid in affective syndromes.** Journal of Nervous and Mental Disease. 158(5):325-330, 1974.

The role of lumbar cerebrospinal fluid (CSF) 5-hydroxyindoleacetic acid (5-HIAA) and homovanillic acid (HVA) in affective syndromes was assessed. Values obtained after administration following probenecid administration reflect composite rates of formation of these acid monoamine metabolites at various sites within the central nervous system. An increase appears in the absolute level of baseline or probenecid induced concentrations of these metabolites in older subjects which may be due to an increase in monoamine oxidase activity with age. In a group of unipolar depressives, pretreatment values of CSF 5-HIAA do not differ from controls, while CSF HVA is increased leading to a decreased 5-HIAA to HVA ratio. Treatment with amitryptyline leads to significant reductions in 5-HIAA and the 5-HIAA to HVA ratio. In bipolar patients, pretreatment values for both metabolites are decreased compared to controls. The values for the 5-HIAA to HVA ratio are elevated. In a group of atypical depressives treated with phenelzine, CSF 5-HIAA and HVA values are consistent with the presence of central monoamine oxidase inhibition. 22 references. (Author abstract modified)

202249 Schildkraut, Joseph J. Neuropsychopharmacology Laboratory, Massachuseets Mental Health Center, Dept. of Psychiatry, Boston, MA 02115 **The effects of lithium on norepinephrine turnover and metabolism: basic and clinical studies.** Journal of Nervous and Mental Disease. 158(5):348-360, 1974.

The effects of lithium on norepinephrine turnover and metabolism were studied. Acute administration of lithium chloride in rats is observed to increase the turnover of norepinephrine in the brain. Further findings suggest that the increase in norepinephrine turnover produced by lithium occurs as result of enhanced intraneuronal release of norepinephrine. In a longitudinal investigation of a manic patient studied prior to treatment with lithium carbonate and for more than 6 months during treatment, a transient increase in the urinary excretion of 3-methoxy-4-hydroxyphenylglycol (MHPG), lasting several days, was observed at the onset of lithium administration; however, subsequently, there is gradual decrease in the excretion of MHPG as well as norepinephrine, normetanephrine, and 3-methoxy-4-hydroxy-mandelic acid (VMA). These findings suggest that long-term effects of lithium on norepinephrine turnover are different from short-term effects. 44 references. (Author abstract modified).

202514 Bastie, Yves. no address /**Eventual developments of 64 chronic psychotics on Moditen Retard or Modecate treatment.**/ Devenir de 64 psychotiques sous Moditen Retard ou Modecate. Annales Medico-Psychologiques (Paris). 1(4):531-536, 1974.

Sixty four psychotics of various specified chronic natures were treated with Moditen Retard or Modecate in order to determine effectiveness, secondary effects and value of usage. Some of the experimental population were in hospital; most were injected by local nurses. Depression and the other secondary symptoms traceable to the drug were corrected with different drugs; corrections were rarely completely successful. The value of these drugs for very intermittent psychotics is questioned and their success with more chronic patients outside hospitals is recommended.

202705 O'Regan, Brian. 803 CN Towers, First Avenue South, Saskatoon, Sask., Canada S7K 1J5 **An M.A.O.I. specific affective disorder. The "too much" syndrome.** Journal of Orthomolecular Psychiatry (Regina). 3(3):152-155, 1974.

A depressive syndrome occurring mainly in premenopausal women which is atypical in that it is characterized by too much sleep, too much eating, too much weight, and possibly too much libido is discussed. Treatment with a monoamine oxidase inhibitor (MAOI) antidepressant is indicated and is always effective. It is important to distinguish other depressive syndromes which may show too much sleep, or too much appetite and too much weight, which may respond to treatment with either MAOI, antidepressants or tricyclic antidepressants. It is suggested that this clinically depressive syndrome is the first described to indicate specific chemotherapy. It is very possible that there may be other syndromes that may be recognized clinically that will also indicate a specific drug treatment. Careful clinical descriptions may well therefore lead to more specific indications for chemotherapy in the affective disorders. 1 reference. (Author abstract modified)

202725 Shader, Richard I.; Jackson, Anthony H.; Dodes, Lance M. Massachusetts Mental Health Center, 74 Fenwood Rd., Boston, MA 02115 **The antiaggressive effects of lithium in man.** Psychopharmacologia (Berlin). 40(1):17-24, 1974.

Since Cade's original suggestions concerning the value of lithium in controlling patients' ungovernable tempers, considerable evidence has accumulated to support this view. The present report reviews this evidence and offers an illustrative case. 19 references. (Author abstract)

202786 Rybakowski, Janusz; Chlopocka, Maria; Kapelski, Zdzislaw; Hernacka, Barbara; Szajnerman, Zofia; Zasprzak, Kazimierz. Psychiatric Clinic, Medical Academy of Poznan, Szpitalna 27/33, Poznan 60-572, Poland **Red blood cell lithium index in patients with affective disorders in the course of lithium prophylaxis.** International Pharmacopsychiatry (Basel). 9(3):166-171, 1974.

Red blood cell (RBC) lithium index (RBC lithium:serum lithium ratio) was estimated in 37 patients with affective disorders in the course of lithium prophylaxis during 4 months. The study revealed no difference in RBC lithium index between patients with manic-depressive psychosis and unipolar depression, as well as between men and women. RBC lithium index was to some extent correlated to the magnitude of serum lithium concentration. The variability of RBC lithium index with time was different in different patients ranging from ±2 to ±50%. The possible importance of RBC lithium index in affective disorders is critically discussed. 11 references. (Author abstract)

202854 Lopez-Ibor Alino, J. J. Clinica Lopez-Ibor, Av. Nueva Zelanda 78, Puerta de Hierro, Madrid 35, Spain **Therapeutic resistant depressions: symptoms, resistance and therapy.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 7(3):178-187, 1974.

Literature, including Freud's case of the Wolfman, on the symptoms of depression, therapy and therapeutic resistant depressions is reviewed, and the need for the therapist to discriminate what type of treatment is best for each patient is stressed. The efficacy of several drugs used to treat endogenous depressions is discussed. It is suggested that it is essential to distinguish in each case the predominance of vital sadness or vital anxiety. Psychosomatic symptoms and affective equivalents, as well as certain vegetative alterations (pupilar diameter, tremor, electroencephalogram), make a good index in the selection of therapies. It is noted that therapists will have to wait for the development of biochemistry to provide a more adequate approach to the prediction of a therapeutic solution. 39 references.

202960 Hordern, Anthony. King's College Hospital, London, England **Depressive disorders.** Practitioner (London). 213(1276):560-573, 1974.

The classification, natural history, biochemistry and diagnosis of depressive illnesses are examined in order to identify problems associated with their treatment. The vast majority of depressive illnesses are well within the capacity of the family doctor to treat, provided he makes the correct diagnosis, prescribes the appropriate drug(s), usually tranquilizing tricyclics, in suitably high dosages for several months and zealously provides followup services. 50 references. (Author abstract modified)

203591 Pichot, P. Centre Psychiatrique Sainte Anne, 100 rue de la Sante, Paris XIVe, France **Therapy resistant depressions: methodological problems. Contributions to methodical questions and animal-experimental aspects.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 7(2):80-84, 1974.

Problems posed by clinical and biological methodology concerning resistance to pharmacological treatment of depression are examined. Two kinds of resistances are defined: resistance concerning a phase of depression and resistance concerning its long-term evolution. Variation in plasma levels of various drugs demonstrate a connection between the plasma level of the drug and the therapeutic clinical effect obtained on the depressive syndrome. However, no unequivocal methodology is proposed.

203592 Coppen, A. MRC Neuropsychiatry Unit, Greenbank, West Park Hospital, Epsom, Surrey, England **The biochemistry of therapy-resistant depression: contributions to biochemistry.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 7(2):85-87, 1974.

The biochemistry of therapy resistant depression is examined. The effects of brain 5-hydroxytryptamine, cerebrospinal fluid 5-hydroxyindoleacetic acid, brain tryptophan and the enzyme tryptophan hydroxylase have a causal relationship to mood. The antidepressant drugs act by increasing the amount of free amine present; the monoamine oxidase inhibitors act by decreasing the rate of catabolism; and the tricyclic drugs act by inhibiting the reuptake of the released amine. Therapy resistant depressions may be due to either or both of two possibilities: drug dosage is not keyed to the biochemical makeup of the patient, and/or the patient may not be taking his medication regularly. Plasma level monitoring is suggested. 15 references.

203593 van Praag, H. M. Div. of Biological Psychiatry, Psychiatric Univ. Clinic, Oostersingel 59, Groningen, Netherlands **Therapy-resistant depressions. Biochemical and pharmacological considerations: contributions to biochemistry.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 7(2):88-97, 1974.

Biochemical and pharmacological considerations of therapy-resistant depressions are presented. The question of why some patients respond to antidepressants while others do not is considered from the metabolic viewpoint. It is felt that factors related to the central monoamine (MA) metabolism exert an influence on the therapeutic efficacy of antidepressants. Application of the probenecid technique in the study of the central MA metabolism in living humans is explained, based on its characteristic to inhibit the transport of acid MA metabolites from the CNS to the blood stream. Questions are discussed as to whether a MA deficiency occurs in depressive patients; if so, is it present in only a proportion of the patients and, if so, can this explain the apparent selectivity of antidepressants in the sense that particularly MA deficient patients benefit from this type of therapy. Implaications for future application of antidepressive agents are discussed. 30 references.

203594 Schildkraut, Joseph J. Massachusetts Mental Health Center, 74 Fenwood Rd., Boston, MA 02115 **Biochemical criteria for classifying depressive disorders and predicting responses to pharmacotherapy: preliminary findings from studies of norepinephrine metabolism. Contributions to biochemistry.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 7(2):98-107, 1974.

Norepinephrine metabolism in patients with affective disorders was examined to find biochemical criteria for classifying patients with different types of depressive disorders and possibly also for predicting differential responses to various antidepressant drugs. The metabolism of norepinephrine within the central nervous system, in urinary excretion, its effects on motor activity and stress, and its metabolic product, 3-methoxy-4-hydroxyphenylglycol (MHPG) are discussed. Studies indicate differences as well as similarities in the neurochemical effects of amitriptyline and imipramine or desmethylimipramine. Preliminary findings suggest that the level of urinary MHPG may provide a clinically useful biochemical criterion for choosing among the tricyclic antidepressants in the treatment of depressive disorders. 55 references.

203596 Pare, C. M. B. Dept. of Psychological Medicine, St. Bartholomew's Hospital, London, E.C. 1 A 7BE, England **Treatment of resistant depression: contributions to genetic aspects.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 7(2):118-121, 1974.

The treatment of resistant depression is discussed. Two factors that contribute to the resistance are identified: that the patient needs an individually tailored dosage of the drugs used; or that the patient's diagnostic category may comprise two or more subgroups, only one of which is responsive to the drug used. 5-Hydroxytryptamine, noradrenaline and dopamine were measured in brains of patients dying from various terminal illnesses and who were receiving monoamine oxidase inhibitors at the time of death. A wide variation in tissue response to tricyclic antidepressants in the brain was found. Patient resistance to antidepressants is found to be dependent on the patient's ability to metabolize the drug and on whether the patient's depression is amenable to the drug used whatever the dose. Research on family members or relatives with depression, and the drugs used to treat the depression is suggested. 20 references.

203600 Best, K.; Kastner, M. Univ. Nervenklinik, 5300 Bonn-Venusberg, Germany **/Lithium therapy in cyclothymia./** Die Lithium-Therapie der Zyklothymie. Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 7(5):237-247, 1974.

The use of lithium in the treatment of affective disorders is reported. Lithium acetate in maintenance therapy was used for 20 patients who had suffered at least two episodes of manic-depressive disorder in the previous years. Of the group, 16 suffered from recurrent manic-depressive disorder, bipolar type, two from recurrent endogenous depressions, unipolar type, and two suffered from schizoaffective disorders. Observations were made for up to 3 years. Significant results were found in the bipolar and monopolar types of manic-depressive disorders, and the schizoaffective psychoses responded well. 64 references. (Author abstract modified)

204392 Consbruch, U.; Orth, M.; Degkwitz, R. Psychiatrische und Nervenklinik der Universitat, 78 Freiburg, Hauptstr. 5, Germany **/Clinical application of lithium aspartate./** Zur klinischen Anwendung von Lithiumaspartat. Arzneimittel-Forschung (Aulendorf). 24(8):1077-1079, 1974.

Serum levels and urinary excretion were monitored in eight healthy subjects receiving a single oral dose of lithium aspartate, and results were compared with the results of earlier experiments on commercial lithium preparations. Lithium applied as the aspartate salt was more slowly eliminated than with the other preparations. Eighteen manic and bipolar manic-depressive patients presenting mainly manic symptoms were treated with lithium aspartate for 7 days to 5 months. Clinical evaluations suggest that Li aspartate is effective in manic patients at about 50% of the dosage needed with other lithium preparations. Effective serum levels of lithium are half those necessary with the commercial salts. Tremors were not observed as side-effects. 4 references. (Journal abstract)

204408 Alino, J. J. Lopez-Ibor; Alino, J. M. Lopez-Ibor. Institut fur neuropsychiatrische Forschung, Av. de Nueva Zelanda no. 78, Madrid-35 **/Psychopharmacological treatment of obsessive syndrome./** Die psychopharmakologische Behandlung von Zwangsneurosen. Arzneimittel-Forschung (Aulendorf). 24(8):1119-1122, 1974.

Psychopharmacological treatment of obsessive syndromes in 29 patients observed from 1966 to 1969 is reviewed. The patients, whose average duration of thymopathic disease was 9.7years, were treated either with chlorimipramine (ChlI) alone or in combination with properiziazine. Infusion therapy with ChlI effected significantly better results than oral treatment. Improvement of obsessional symptoms occurred after 20-40 days. Out of the 29 patients, 13 became free of symptoms, 13 improved and three remained unchanged. Seven in the improved group became free of symptoms in the following 4 years. In 50 patients, it was found that the daily dose of ChlI and properiziazine should be as high as possible, limited only by the constancy of mydriasis and the palmomental reflex. A maintenance dose over several years is recommended. The drugs seem to dissolve the anancastic defense by anxiolytic action. 58 references. (Journal abstract modified)

204411 Voelkel, A. Neuropsychiatrische Klinik Waldhaus, 1 Berlin 38, Am Waldhaus 1-19, Germany **/The activity profile of piracetam in psychosyndromes and symptomatic psychoses./** Uber das Wirkungsprofil von Piracetam bei Psychosyndromen und symptomatischen Psychosen. Arzneimittel-Forschung (Aulendorf). 24(8):1127-1129, 1974.

The encephalotropic drug effect of piracetam as seen in patients with different reversible encephalopathic psychosyndromes combined with depressive or paranoid syndromes is described. A pilot study shows that the most important effect is a remarkable restoration of memory, vigilance, lucidity and differentiation. Piracetam also provokes psychotic reactions with paranoid symptoms and hallucinations in cases with uncertain subclinical, endogenous, psychotic syndromes with dissimulation. 19 references. (Journal abstract modified)

205155 Davies, Brian. University of Melbourne, Australia **Recent advances in the treatment of depression.** Indonesian Psychiatric Quarterly (Djakarta). 7(1):105-112, 1974.

Recent advances in the treatment of depression are reviewed. The areas of advancement are categorized as to recognition and diagnosis of a depressed patient, physical symptoms and signs of depressive illness and an overview of the mental state and behavior of depressed patients. Treatment of the depressed patient is advancing toward more realistic acceptance of depression as a real illness by the medical profession. In the pharmacological treatment of depression, antidepressants and not antianxiety drugs are becoming the treatment of choice. The prevention of recurring depressive and/or manic episodes has advanced therapeutically in the last few years with the treatment of lithium. (Author abstract modified)

205318 Kiloh, L. G.; Neilson, Megan; Andrews, Gavin. School of Psychiatry, University of New South Wales, Prince Henry Hospital, Little Bag, N.S.W. 2036, Australia **Response of depressed patients to methylamphetamine.** British Journal of Psychiatry (London). 125:496-499, 1974.

Thirty-nine patients with endogenous depression and 56 with neurotic depression were given 15mg methylamphetamine intravenously to determine the difference in response of the two groups to the drug. There was a strong tendency for all patients to feel better, irrespective of diagnosis. No significant difference was found between the responses of patients with neurotic and those with endogenous depression, nor was any significant relationship established between prognosis on discharge from hospital and 6 months later in any diagnostic group. The response to intravenous methylamphetamine appeared to have no diagnostic or prognostic significance in patients with depressive illness. 15 references. (Author abstract modified)

205580 Svestka, J.; Nahunek, K.; Roduva, A. Psychiatric Clinic, BrnosBohunice, Jihlavska 102, Czechoslovakia **Experience with oxyprothepine in the treatment of manic syndromes.** Activitas Nervosa Superior (Praha). 16(3):162-163, 1974.

At the 16th Annual Psychopharmacological Meeting, oxyprothepine treatment in manic syndromes of affective psychoses for which neuroleptics are frequently indicated was reported. The results of 35 treatments in 33 patients are presented. The basic symptoms of the manic syndrome were rapidly and well influenced. In schizo-affective psychoses therapy acted well on hallucinations, delusions and thinking. In 4 patients there was a slight reversal to subdepression with heightened anxiety. Treatment of insomnia resulted in a reversal to hypersomnia, especially in the group of successful patients, which may serve as a favorable prognostic sign in practice. An evaluation of side-effects showed an affinity of oxyprothepine to the autonomic as well as extrapyramidal system. It was concluded that oxyprothepine after its previous good results in schizophrenic psychoses proved to be also a good antimanic drug and due to 57% full and 29% partial remission occupies the same place as the most successful compounds indicated for these types of psychoses. 3 references.

205589 Dolezalova, V.; Faltus, F.; Soucek, K. Psychiatric Clinic, Praha 2, Ke Karlovu 11, Czechoslovakia **Pilot clinical study with trifluperidol (Trisedyl) therapy in psychotic patients.** Activitas Nervosa Superior (Praha). 16(3):171, 1974.

At the 16th Annual Psychopharmacological Meeting, the effects of Trisedyl, administered to 20 hospitalized schizophrenic patients for a period of 4 weeks, were reported. Eight patients were treated in their first attack, 12 at an exacerbation of the chronic course. All patients in the first group improved, 87.5% very markedly, in the symptoms assessed polarly and unpolarly. The chronic patients showed improvement primarily in symptoms that were assessed polarly, the basic psychotic symptoms improved only in 50%, in the rest of the patients the chief psychotic manifestations were mitigated or remained unchanged. Therapy was least effective in the two paraphrenias. In both patient groups the effect was most pronounced on symptoms assessed polarly. The improved symptoms assessed polarly were most marked in patients suffering their first attack. The results were best in delusion, hallucination, insight and anxiety.

205600 Nahunek, K.; Kamenicka, V.; Ceskova, E.; Rodova, A.; Svestka, J.; Misurec, J. Psychiatric Clinic, Brno-Bohunice, Jihlavska 102, Czechoslovakia **Clinical experience with doxepin.** Activitas Nervosa Superior (Praha). 16(3):185-186, 1974.

At the 16th Annual Psychopharmacological Meeting, the results of doxepin treatment applied to 66 patients suffering from endogenous and involuntary depression were reported. A total of 45.4% full and 21.2% partial remissions were achieved. The bipolar activity of the drug revealed itself in balanced results in inhibited forms of depression (50%) and in anxious forms (53.7% of full remissions). The results in atypical forms were somewhat slighter (29.4%). On average the results were more satisfactory in patients with a lower initial intensity of psychopathological symptoms. The onset of the therapeutic effect was apparent in most cases after the first week of treatment. Doxepin was as a rule effective in basic depressive symptomatology. The influence on the hypochondric, obsessive and paranoid hallucinatory component which was present in a small number of patients, was less satisfactory. 4 references.

10 DRUG TRIALS IN NEUROSES

198078 Covi, Lino. Johns Hopkins University, Baltimore, MD **NIMH-PRB outpatient treatment of depression.** Psychopharmacology Bulletin. 10(2):56, 1974.

The relative effectiveness and interactions of an antidepressant (imipramine), a minor tranquilizer (diazepam), and a placebo in the treatment of neurotically depressed women who are receiving either group therapy or minimal contact supportive therapy in conjunction with the drug therapy is evaluated. The effects of withdrawing drugs and of using the same doctors to administer all forms of treatment is also being studied. Maintenance treatment on medication for improved patients will be evaluated. Implications for an increased understanding of the differential effects of antidepressants and minor tranquilizers in treating neurotics and the value of combined pharmacotherapy and psychotherapy are discussed. (Journal abstract modified)

198079 DiMascio, Alberto. Tufts University, Boston, MA **Drug therapy of depressed outpatients.** Psychopharmacology Bulletin. 10(2):57, 1974.

The effects of psychotherapy and amitriptyline in the treatment of depressed patients are examined, in order to determine the length of time patients should stay on this drug, the probability of relapse and the relative efficacy of the drug and psychotherapy. The depressed patients will be placed on amitriptyline for 4 weeks to secure the sample. Those who respond will enter a maintenance dose period of 100mg per day for 8 weeks. The information collected will cover social and clinical data and incidence of relapse. (Journal abstract modified)

198083 Prusoff, Brigitte. Yale University School of Medicine, New Haven, CT **Drug treatment of depressed outpatients.** Psychopharmacology Bulletin. 10(2):59-60, 1974.

The usefulness of amitriptyline, combined with psychotherapy, in preventing relapse in depressed patients was studied. A significant portion of the patients could not tolerate cessation of the experimental phase of the study, and they requested or insisted upon continued treatment. Amitriptyline treatment was the main factor that accounted for prevention of relapse. (Journal abstract modified)

198087 Goldstein, Burton J. University of Miami, Coral Gables, FL **Patient profiles and differential response to drugs.** Psychopharmacology Bulletin. 10(2):61-62, 1974.

The relative effectiveness of the antidepressants, imipramine and diazepam, is studied in order to pinpoint various factors, such as personality and background, that affect patients' response to drugs. Before, during, and after a double-blind treatment with certain drugs physician's rating and self-rating of symptoms will be computerized and analyzed. In preliminary studies using symptomatic volunteers, the subjects treated with imipramine and diazepam responded differently than those receiving a placebo. (Journal abstract modified)

198092 Dahlberg, Charles C. William Alanson White Institute, New York, NY **Effects of LSD-25 on psychotherapeutic communication.** Psychopharmacology Bulletin. 10(2):64-65, 1974.

The effects of LSD-25, dextroamphetamine, and placebo on verbal interaction in psychotherapy were studied. The subjects were neurotic, White middle-class men and women between the ages of 23 and 43. As compared to placebo, d-amphetamine decreased average pause time and LSD in-

creased it. The typical LSD patient was more intolerant of interruption, regardless of whether the patient was withdrawn and silent or talkative and excited. LSD diminished interpersonal relatedness and led to greater autonomy. LSD produced greater emotionality as measured by crying. The ability to understand language per se was not changed by LSD or dextroamphetamine. (Journal abstract modified)

198099 Rosenblatt, Seymour. Mount Sinai School of Medicine, New York, NY **Biochemical monitoring in the therapy of depressions.** Psychopharmacology Bulletin. 10(2):67, 1974.

Biochemical monitoring is being used to establish pretreatment norms in the therapy of depressions. The individual norepinephrine (NE) reuptake curves are determined by administering a minute dose of radioactive NE and assessing the distribution of amine and oxidized metabolites (N/O ratio) in a urine specimen collected from 12 to 20 hours later. Psychiatric assessments are made and patients judged to be drug-free are administered either imipramine or amitriptyline. N/0 ratios are determined on a regular basis, with the objective of providing a scientifically precise biochemical measurement technique in the field of drug research. (Journal abstract mdofied)

198100 Satterfield, James H. Gateways Hospital, Los Angeles, CA **EEG changes with lithium in depressed patients.** Psychopharmacology Bulletin. 10(2):68, 1974.

The effects of long-term use of lithium carbonate and amitriptyline on the EEG responses of depressed patients are being studied. Psychiatric patients who have experienced at least two manic-depressive episodes within a 2-year period are the subjects. Lithium increased the amplitude of the auditory evoked response potential and decreased recovery time. There was a shift of EEG energy patterns to slow frequencies. (Journal abstract modified)

198354 Katicic, N. Psychiatric Department with the Centre for Mental Health of the Medical Faculty, Zagreb, Yugoslavia **/Work capability and treatment of reactive depressions./** Radna sposobnost i lijecenje reaktivnih depresija. In: Persic, N., Socijalna Psihijatrija. Zagreb, Pliva, 1971. 823 p. (p. 617-621).

The relationship between emotional exhaustion and appearance of reactive depressive conditions is examined. After a number of years, such conditions have arisen in rather good working women. Their work posts have not been hard but have been monotonous. The family factor and situation, as well as a series of additional work post stresses, have represented a major etiological factor. In all of the cases, a suggestive psychotherapy has been carried out. The patients have also been treated with peroral antidepressants. Conditions have improved. 8 references. (Journal abstract modified)

198396 Gruden, V. Psychiatric Department with the Mental Health Center, Medical Faculty, Zagreb, Yugoslavia **/Tacitin and Aponal in the treatment of neuroses./** Tacitin i Aponal u lijecenju neuroza. In: Persic, N., Socijalna Psihijatrija. Zagreb, Pliva, 1971. 823 p. (p. 814-819).

The effects of Tacitin and Aponal on neuroses were reported. Tacitin was effective against insomnia, cardiovascular psychovegetative disturbances, irritability, aggressiveness, anxiety and inner tension, while Aponal proved itself extremely effective against anxiety, tension, rigidity, depression and insomnia. Side-effects were noted only in a few patients. Both Tacitin and Aponal can be used in combination with psychotherapy. No signs of addiction were noted on prolonged application of either of the two drugs. 6 references. (Journal abstract modified)

199991 Dasberg, H.; Van Praag, H. M. Department of Biological Psychiatry, University of Groningen, Groningen, the Netherlands **The therapeutic effect of short-term oral diazepam treatment on acute clinical anxiety in a crisis centre.** Acta Psychiatrica Scandinavica (Kobenhavn). 50(3):326-340, 1974.

The assumption that oral diazepam treatment (20mg daily) during 5 days in combination with active inpatient crisis intervention has a favorable effect on acute clinical anxiety states was examined. A simple double-blind random placebo-diazepam design was applied on 30 crisis patients. The evidence derived from totals of Hamilton scales, nurse scales, and visual analogue scales does not support the assumption that diazepam is therapeutically better than placebo if one compares the two medication groups as units. But for the subgroup of patients with the highest levels of pretreatment anxiety, a short-term administration of oral diazepam seems to be a valuable adjunct to a crisis intervention program. Diazepam has a selective action for the improvement of insomnia, respiratory and gastrointestinal complaints. Diazepam or some factor connected with it has an adverse influence on some autonomous complaints. 32 references. (Author abstract modified)

200238 Behavioral Sciences Tape Library, c/o Sigma Information, Inc., 240 Grand Avenue, Leonia, NJ 07601 (201-947-4154) BST (S)$7.95 ea. **Uses of Psychotropic Drugs.** AT 1 7/8 IPS cassette 60 min ea., 1974.

A clinically-oriented discussion of practical aspects in the use of psychotropic drugs is presented by Dr. David W. Wheatly of the General Practitioners Research Group, Middlesex, England. Emphasis is on the use of drugs in private practice, and on techniques for achieving maximum results in anxious and depressed patients in the office care setting. The individual tape titles are: 1) Psychotropic drugs in private practice; 2) Drugs for the anxious patient; and 3) Drugs for the depressed patient.

201896 Bonn, J. A. Dept. of Psychiatry, St. Bartholomew's Hospital, London EC1, England **Progress in anxiety states.** Proceedings of the Royal Society of Medicine (London). 66(3):249-252, 1973.

The development of a therapeutic behavioral technique for the treatment of free-floating anxiety is reported. The flooding technique with sodium lactate infusion involved the rapid arousal of maximal anxiety either by a reality situation or in imagination. It has been shown to be more effective than desensitization. Experiences with beta-adrenergic blocking agents have shown that DL-propranolol given in adrenergic receptor blocking doses to patients with anxiety and particularly its somatic manifestations, produces significant improvement. A controlled study which compared the effects of practolol and placebo was made with patients with severe and intractable anxiety. The drug was found to have a beneficial effect on anxiety also. It is suggested that somatic symptoms referable to the cardiovascular system occur in the majority of anxious patients even though routine questioning may fail to elicit them. 16 references.

201897 Kelly, Desmond. St. George's Hospital Medical School, Atkinson Morley's Hospital, London SW20 0NE, England **Progress in anxiety states.** Proceedings of the Royal Society of Medicine (London). 66(3):252-255, 1973.

The use of minor tranquilizers in the treatment of anxiety states is discussed. The benzodiazepines are one of the most widely used groups of psychotropic drugs and they appear to be useful in reducing the background level of anxiety and can be effective sedative agents for overcoming acute anxiety. Studies with diazepam, chlordiazepoxide, oxazepam, medazepam, benzoctamine and the phenothiazines are discussed. Studies with antidepressants and monoamine oxidase inhibitors for treating anxiety states are also reported. The use of tricyclic antidepressants, combined antidepressants, modified narcosis and limbic leucotomy are also examined. 17 references.

202178 Tanimukai, Hiroshi; Inui, Masashi; Kaneko, Ziro. Department of Neuropsychiatry, Osaka University Medical School, Osaka, Japan **A double-blind comparison of clomipramine with amitriptyline in depression.** Clinical Psychiatry (Tokyo). 13(6):625-633, 1971.

The effects of clomipramine and amitriptyline on depression were studied in a double-blind trial. Clomipramine was effective in 89.5% of patients and amitriptyline in 90.5%. Side-effects of both drugs included tachycardia, dry mouth, perspiration, digestive disturbance, dizziness and drowsiness. 30 references.

202219 Kerry, R. J.; McDermott, C. M.; Orme, J. E. Northern General Hospital, Sheffield, S5 7AU England **Bromazepam, medazepam, chlordiazepoxide in treatment of neurotic anxiety.** British Journal of Psychiatry (London). 124:485-486, 1974.

Bromazepam, medazepam, and chlordiazepoxide in the treatment of neurotic anxiety were evaluated. A new benzodiazepine, bromazepam, 6mg three times a day was compared in a double-blind trial with medazepam, 10mg three times a day and with chlordiazepoxide, 10mg three times a day. Each drug was given for 2 weeks. The first 50 cases attending the outpatient department were selected. All suffered from neurotic anxiety and were comparable to those patients for whom sedation is generally prescribed. The patient was assessed and changes rated by the same doctor at fortnightly intervals using a scale previously published by Jenner, Kerry and Parkin in 1961. Medazepam proved most successful in symptom relief, followed by bromazepam, then chlordiazepoxide. Unfortunately, positional effects were evident in the therapeutic course. Indications for use of individual drugs are presented. The patient was maintained on his most helpful drug. 5 references. (Author abstract modified)

202390 Notosoedirdjo, Moeljono. Department of Psychiatry, Airlangga University, Surabaya, Indonesia **Recent advances in the treatment of depression.** Bandung, Indonesian Society for Neur., Psych. & Neurosurgery, 1973. 5 p.

Symptoms and etiology of depressive illness are briefly reviewed, and the organic biological approach to treatment is discussed. Common psychotropic drugs useful in depression are outlined, with emphasis on lithium. 6 references.

204428 Fujita, Chihiro. no address **Therapeutic roles of drugs and Morita therapy process.** Practice and Theory of Psychotherapy (Tokyo). 5(2):17-28, 76, 1974.

Drug therapy and psychotherapy in the treatment of neurosis in Morita therapy are discussed. Although the use of drugs for treatment of neurosis is increasing, the therapist should not rely on the use of drugs alone or make a choice between somatotherapy and drug therapy, as in the past. The preferable therapeutic system is a combination of drug therapy and psychotherapy. The therapeutic situation varies according to the type of case, but the goal is the acquisition of individual freedom and self-realization, which can be attained by the mutual action of drugs and psychotherapy. The purpose of drugs, time of administration and period of use are discussed. 7 references. (Author abstract modified)

204464 Shimizu, Hidetoshi. Zentsuji National Hospital, Kagawa, Japan **Clinical trial of clocapramine in neurotic patients who had troubles in everyday life owing to severe anxiety, irritability and depression.** Iryo (Therapeutics) (Tokyo). 27(9):773-779, 1973.

A clinical trial of clocapramine with 15 neurotic patients who had troubles in daily life owing to severe anxiety, irritability, hypochondria and depression is reported. The drug was administered daily for from 7 to 300 days. Results indicate that three subjects showed a very good effect, seven showed good effects, three showed moderate effects and in two subjects there was no effect. The drug was effective for three cases of hysteria, four out of five cases of anxiety neurosis and against all three cases of depressive neurosis. Side-effects included sleep disturbance, Parkinson's syndrome, blood pressure reduction, mouth dryness and visual disturbance. The drug is effective in the treatment of anxiety, irritability, hypochondria and depression. 5 references. (Author abstract modified)

204899 Angst, J.; Koukkou, Martha; Bleuler-Herzog, Marianne; Martens H. Psychiatrische Universitatsklinik, Forschungsdirektion, Postfach 68, CH-8029 Zurich, Switzerland **/Results of an open and a double-blind study of Nomifensine in comparison to Imipramine./** Ergebnisse eines offenen und eines Doppelblindversuches von Nomifensin im Vergleich zu Imipramin. Archiv fur Psychiatrie und Nervenkrankheiten (Berlin). 219(3):265-276, 1974.

In an open study 20 depressive patients were treated with Nomifensine in daily doses of 50 to 100mg. In a double-blind study, 15 depressive patients were treated with Nomifensine (150mg per day) and 15 with imipramine (150mg per day). Treatment was continued for a maximum period of 30 days. The patients tolerated both substances well and side-effects were observed only infrequently. Both substances had a significant antidepressive effect. The therapeutic profile of Nomifensine and imipramine demonstrated no significant differences. In a symptom-by-symptom analysis, initial effects of Nomifensine were observed on day 10; there was almost no difference on day 20, and on day 30 imipramine showed a trend toward a better therapeutic effect. However, this last observation is based on a small number of cases. Both substances were found to have the identical antidepressive effect on the following AMP syndromes: apathy, somatic depressive S, retarded depressive S, hypochondriasis, and psychoorganic S. The onset of a thereapeutic effect was equally quick with both drugs, and as a rule it became significant after day 10. Thus both substances can be considered as efficient antidepressive drugs. 3 references. (Journal abstract modified)

205598 Rydzynski, Z.; Duszyk, S.; Sklodowski, H. Psychiatric Dept., Medical Military Academy, Lodz, Poland **Limbitrol in out- and in-patients practice.** Activitas Nervosa Superior (Praha). 16(3):184, 1974.

At the 16th Annual Psychopharmacological Meeting, the effects of Limbitrol in the treatment of an anxious-depressive condition of a neurotic origin were reported. The improvement began in 2-3 days of treatment with sedation and regulation of sleep. Next, clinical symptoms of anxiety disappeared, the mood improved, the patient began to control himself and

became more susceptible to psychotherapy. Improvement, however, was rather superficial and anxiety and depression were more blocked than cured.

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

198085 Conners, Carmen K. Massachusetts General Hospital, Boston, MA **Drug and cognition studies in disturbed children.** Psychopharmacology Bulletin. 10(2):60-61, 1974.

Effects of the stimulants dextroamphetamine, methylphenidate, and diphenylhydantoin on the behavior of brain-damaged children and children with conduct and/or learning problems were studied. Dextroamphetamine improved paired-associate learning, continuous performance tests of attention, Porteus Maze performance, ratings of activity level, and ratings of academic performance, but it did not affect improvement on other tests. It is concluded that dextroamphetamine primarily affects functions of attention rather than memory or perception. In general, children with minimal brain damage responded more favorably than unimpaired hyperactive children, possibly due to the hyperactives' faster metabolic rates. (Journal abstract modified)

198089 Pillard, Richard C. Boston University, Boston, MA **Anxious dental patients as models of psychopathology.** Psychopharmacology Bulletin. 10(2):63, 1974.

The stress-reducing properties of tranquilizing or sedating drugs, a benzodiazepine tranquilizer, a barbiturate, or a placebo, on anxious dental patients are examined. A variety of psychological questionnaires and a measure of the subject's state of arousal (finger sweat) are administered at various times before, during, and after the cleaning procedures. The effects of the drug treatment on reducing anxiety are assessed. (Journal abstract modified)

198090 Rapoport, Judith L. Georgetown University Medical School, Washington, DC 20007 **Comparative drug treatment of hyperactive children.** Psychopharmacology Bulletin. 10(2):63-64, 1974.

The long-term and short-term effects of stimulants and antidepressants on the behavior, cognitive performance, and clinical outcome of minimal brain dysfunction (MBD) children are studied using White, middle-class children, aged 6 to 13. Subjects are assigned randomly to a methylphenidate, imipramine, or behavioral therapy group for 1 year, after which unresponsive subjects are switched to other treatment procedures. (Journal abstract modified)

198091 Sprague, Robert L. University of Illinois, Urbana, IL **Pediatric psychopharmacology.** Psychopharmacology Bulletin. 10(2):64, 1974.

The effects of the stimulant methylphenidate (Ritalin) and the depressant thioridazine (Mellaril) on memory and learning processes, activity, and physiological responses are studied. Subjects are retarded and emotionally-disturbed children 4 to 12 years old. Rats are used in laboratory experiments to test the effects of methylphenidate on the formation of the myelin sheath in associative areas of the cortex. Results may provide a better basis for clinical evaluation of the effectiveness and safety of psychotropic drugs for treating children's emotional and behavioral problems. (Journal abstract modified)

198394 Uglesic, B.; Dragicevic, D. Neurological and Psychiatric Department of the General Hospital, Split, Yugoslavia /**Sociopsychiatric significance of the application of psychotropics in geriatrics.**/ Socijalnopsihijatrijsko znacenje primjene psihofarmaka u gerijatriji. In: Persic, N., Socijalna Psihijatrija. Zagreb, Pliva, 1971. 823 p. (p. 805-808).

The role of psychotropics in geriatric treatment was studied. Results are given concerning possible action in geriatric psychohygiene provided by the combination of Progresin and Revibol. This combination seems to inhibit the first symptoms of slowed mental activity and loss of vitality, and to enable patients to maintain a normal life rhythm for a prolonged period of time. The therapy is well tolerated and has no serious contraindications. 11 references. (Journal abstract modified)

198395 Hancevic-Rajakovic, N. Vrapce Psychiatric Hospital, Zagreb, Yugoslavia /**Revibol in children's psychiatry.**/ Revibol u djecjoj psihijatriji. In: Persic, N., Socijalna Psihijatrija. Zagreb, Pliva, 1971. 823 p. (p. 809-813).

The use of Revibol in treating children suffering from superficial neuroses with conversion, neurasthenic and phobic symptomatology was studied. Revibol showed a beneficial effect on some symptoms of the psychoorganic syndrome. It was not effective against deeply-fixed neuroses, delinquent behavior, or states caused by insoluble family problems and many other long-term frustrations. Revibol had a specific effect on enuresis of organic origin and was a successful adjutant in the treatment of educationally neglected children and children with poor performance at school. 8 references. (Journal abstract modified)

198423 Coleman, Mary. Children's Neurological Research Clinic, Washington, DC **Serotonin in Down's syndrome.** New York, American Elsevier, 1974. 224 p. $15.50.

The effect of raising serotonin levels in Down's syndrome patients whose mental retardation is associated with one or more chromosome errors is studied. Newborn values of serotonin in normal children are described, and this pattern of normal values is then contrasted to the lower values seen in the Down's syndrome patients. A double-blind interdisciplinary study of patients given 5-hydroxytryptophan (5HTP) or a placebo from the first week of life until 3 years of age is included. Patients were evaluated by a neurologist, psychiatrist, psychologist and by a specialist in the electroencephalogram (EEG). Studies of mental function, motor function, behavior patterns, EEG, temperature, strabismus, tongue protrusion, cardiac diseases, growth patterns and the biochemistry of the patients were completed. The effect of other agents on serotonin levels in Down's syndrome patients is described. Vitamin B6, tryptophan, tranylcypromine and imipramine studies are reported. The serotonin syndromes of infancy are described.

198662 Jacobson, Ruth Sarah Forman. Boston University School of Education **A comparison of the relative efficacy of special class education and drug therapy for children with selected learning disabilities. (Ed.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-20439 HC$12.50 MF$4.00 259 p.

To examine the contention that hyperactive children are a heterogeneous group and that their responses to stimulant drug treatment cannot be related to the apparent etiology of hyperactivity, carefully selected medical and educational procedures were used to evaluate the effects of methylphenidate (Ritalin) on 13 hyperactive, learning disabled subjects attending a special class in one school for 2.5hours every day for one complete school year. Stimulant drugs

specifically affected hyperactive behaviors by reducing excessive inappropriate behaviors as observed by independent raters and a special class teacher. Ritalin facilitated improvement in performance in arithmetic computation. Parents, whose observations occurred outside of school hours, did not observe beneficial effects of Ritalin. Ritalin was effective as one of several possible variables in management of hyperactive, learning disabled subjects. (Journal abstract modified)

198705 Wakahara, Takao; Kamiya, Ikuo. Kyoritsu Kikukawa Hospital, Japan **Comparative study of Y-6047 and diazepam by a double-blind method for the treatment of psychosomatic diseases and neurosis.** Medical Consultation and New Remedies (Tokyo). 10(9):2063-2074, 1973.

The effects of Y-6047 and diazepam (Dz) on psychosomatic diseases and neuroses were studied in a double-blind test of 80 inpatients and outpatients with complaints of insomnia, headache, heaviness in the head, pressure in the chest and unpleasant feeling in the stomach, all of which were considered to be induced by anxiety and tension. Subjects were treated with Y-6047 or Dz for 2 weeks. Among the 80, 32 outpatients dropped out of the test. Among 48 patients who completed the test, three showed remarkable improvement, 17 showed fairly good improvement, 19 showed some improvement, and nine showed no change. Rate of effectiveness was the same for both drugs, but they showed a statistically significant difference in the distribution of the effect. Y-6047 was slightly more effective in feelings of anxiety. Side-effects are noted. 6 references.

199473 Moldofsky, Harvey; Tullis, Carol; Lamon, Richard. Clarke Institute of Psychiatry, 250 College Street, Toronto 2b, Ontario, Canada **Multiple tic syndrome (Gilles de la Tourette's syndrome): clinical, biological, and psychosocial variables and their influence with haloperidol.** Journal of Nervous and Mental Disease. 159(4):282-292, 1974.

Biological and psychosocial variables related to multiple tic syndrome and the manner in which they contribute to the varying responses to haloperidol were investigated. Responders to haloperidol who have a family history of tics may suffer from a genetic and metabolic disorder, whereas nonresponders, who are inclined to perinatal abnormalities and have a later onset of tics, have an acquired disorder. Behavioral disturbances and psychosocial adaptation may influence or be influenced by drug usage. The hypothesis of uric acid metabolic abnormality was not supported but dopaminergic and/or gamma-hydroxybutyrate neural systems may be implicated. 34 references. (Author abstract modified)

199640 Feinberg, Irwin; Hibi, Satoshi; Braun, Madeleine; Cavness, Cleve; Westerman, George; Small, Arthur. Veterans Administration Hospital, 4150 Clement St., San Francisco, CA 94121 **Sleep amphetamine effects in MBDS and normal subjects.** Archives of General Psychiatry. 31(5):723-731, 1974.

Altered sleep patterns were assessed in minimal brain dysfunction syndrome (MBDS or hyperkinesis) children under amphetamine treatment compared to age-matched controls. Electroencephalographic sleep patterns in children with MBDS before and during stimulant treatment differed little from those of age-matched controls. It is unlikely that the therapeutic mechanisms of amphetamines in MBDS are exerted on or reflected in physiological sleep patterns. Neither MBDS children nor normal young adults showed withdrawal elevations of rapid eye movement (REM) sleep after administration of amphetamines in constant dosage. Young adults showed REM rebounds only when the dosage was increased prior to withdrawal. In contrast to sedative hypnotics, stimulant drugs do not reduce eye movement activity during REM sleep. This difference is emphasized for the specificity hypothesis--that different classes of psychoactive drugs differentially alter physiological sleep patterns--would be untenable if sedatives and stimulants produced the same effects on sleep. 31 references. (Author abstract)

200009 Kobayashi, Toshino; Ohta, Yoshitaka; Suda, Takeko; Yamaguchi, Kuniko; Ishida, Takashi; Asao, Hirokazu; Nanno, Hisashige. Osaka Prefectural Public Health Center, Japan **Clinical pharmacological study of a hypnotic drug, Tricloryl.** Osaka Furitsu Koshu Eisei Kenkyusho Kenkyu Hokoku (Osaka). 12:99-104, 1974.

The hypnotic effect of Tricloryl on children was examined, based on EEGs recorded during sleep of 36 2 to 4-year-old healthy children and 59 2 to 9-year-old children with linguistic disturbance, brain damage, emotional disturbance and abnormal behavior, all of whom were treated with the drug Tricloryl. Results show that those in the disturbed group fell asleep more quickly after drug treatment than did the normals, especially those who had exhibited abnormal EEGs. The disturbed group was also more likely to exhibit deep sleep at the beginning of their sleep periods. It is concluded that the hypnotic action of tricloryl is strongest in children with organic brain damage. 6 references.

200104 Prokudin, V. N.; Raiskiy, V. A.; Romanov, Yu. D. Moscow Institute of Psychiatry, Moscow, USSR /A **differentiated use of elenium and seduxen in young patients in the post-infarctional period.**/ O differexntsirovannom primenenii eleniuma i seduksena u bol0nikh molodogo vozrasta v postinfarktnom periode. Zhurnal Nevropatologii i Psikhiatrii Imeni S. S. Korsakova (Moskva). 74(2):282-288, 1974.

The effects of elenium and seduxen on patients in the postinfarctional period were studied. The patients were 80 males under 45 years of age. Best results were attained in patients with neurotic symptoms in the premorbid personality and stable pseudoneurotic conditions formed after infarction. This treatment was less effective in psychopathic disorders prior to infarctions and in psychopathic disorders with a prevalence of hypochondriacal and asthenical conditions which followed infarctions. In conditions of expressed excitability and irritability and insomnia, the most efficacious treatment was attained with small doses of elenium (15-30mg daily). In asthenic states, increased fatigability and apathy, the optimal effect resulted from small doses of seduxen (5-12mg daily). 22 references. (Journal abstract modified)

200170 Galassi, G.; Aguilar, C. L. Clinica delle Malattie Nervose e Mentali dell'Universita di Modena, Modena, Italy /**Clinical observations on sulpiride treatment in psychiatry.**/ Esperienze cliniche con il sulpiride in terapia psichiatrica. Rivista di Patologia Nervosa e Mentale (Firenze). 94(1):1-28, 1974.

A recently synthetized drug (sulpiride) is described in its chemical, pharmacological and toxicological properties. A clinical trial on 50 psychiatric patients is discussed. The use of sulpiride alone or in association with classical antidepressant drugs is advisable in depressive states with mild anxiety, but its administration should be avoided in states of excitement. It is suggested that this drug is among the major neuroleptics because of its powerful antipsychotic activity in hallucinated patients and beneficial effects also in chronic schizophrenic psychoses of long standing. 42 references. (Author abstract)

200461 Layman, Dale Elton. Georgia State University - School of Education **A behavioral investigation: the effects of medication on disruptive classroom behavior and academic performance. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-23175 HC$12.50 MF$4.00 79 p.

The separate effects of medication and behavioral intervention, disruptive classroom behavior and academic achievement were systematically observed. Results show that medication does affect classroom disruption in that, upon the removal of medication, classroom disruption increased. Academic performance was positively affected by the removal of medication; each child increased daily percent correct while off medication, disregarding the marked increase in hyperactive or disruptive behavior. Introduction of a behavioral contingency system increased academic performance for all subjects to a level of 85% correct each day in each subject. The findings show each individual's ability to perform academically and behaviorally in an acceptable manner without medication. (Journal abstract modified)

201496 Riklan, Manuel. Fordham University, Bronx, NY **L-dopa and parkinsonism: a psychological assessment.** Springfield, IL, Charles C Thomas, 1973. 416 p. $15.75.

The existing behavioral literature, and some of the known biochemical, pharmacological and physical aspects of L-dopa are reviewed. The existing data are reassessed in an effort to better understand the behavioral consequences of L-dopa therapy for the parkinsonian.

201690 Gentili, P. Universita degli Studi di Roma, Facolta di Medicina e Chirurgia, Rome **/Bromazepam in treating dysthymic elderly patients./** Il bromazepam nel trattamento di pazienti anziani distimici. Giornale di Gerontologia (Firenze). 22(7):457-466, 1974.

Fifty-two female dysthymic senile patients were administered bromazepam in a preliminary open trial and a double-blind trial within 30 days. The drug was found to have a therapeutic effect on many dysthymic symptoms, such as anxiety, tension, irritability, excitability, obsessions, and sleep disturbances. Improvement was greater with bromazepam than with placebo. Positive results with the placebo were mostly in the middle categories of seriousness; the positive effects obtained with the placebo were explained with special attention to the particular conditions of the patients and the different etiology of dysthymic symptoms. 4 references. (Journal abstract modified)

201694 Hauser, G. A.; Wenner, R. Frauenklinik de Kantonsspital, CH-6004, Lucerne, Switzerland **/Reserpine therapy for menopausal trouble./** Reserpintherapie bei klimakterischen Beschwerden. Therapeutische Umschau (Revue Therapeutique) (Bern). 31(3):179-181, 1974.

Serpasil was investigated as a therapeutic agent in menopausal troubles. It was found that Serpasil, even in small doses, is effective in 80% of women with menopausal manifestations of endocrine deficiency and that complete relief is obtained in at least half the cases. Coexistent circulatory disorders in the hands, as well as mastopathies, suggest that no effect should be expected. The earlier the menopause sets in, the better the response to Serpasil. The best response is obtained in cases presenting with sleep disorders or labile hypertonia. Normal blood pressure is no contraindication. 5 references. (Journal abstract modified)

201870 Browne, Thomas R.; Penry, J. Kiffin. National Institute of Neurological Diseases and Stroke, National Institutes of Health, Bethesda, MD 20014 **Benzodiazepines in the treatment of epilepsy: a review.** Epilepsia (Amsterdam). 14(3):277-310, 1973.

The anticonvulsant effect of benzodiazepines is reviewed, both on experimentally-produced seizures and on epilepsy in man, including aspects of clinical pharmacology and toxicology. The drugs are chlordiazepoxide (Librium), diazepam (Valium), oxazepam (Serax), nitrazepam (Mogadon), and clonazepam. Flurazepam (Dalmane) has not been tested extensively. The benzodiazepines suppress generalized electroencephalogram (EEG) discharges but not focal ones. They are highly effective in stopping absence (petit mal), infantile and other myoclonic seizures, akinetic, photosensitive and alcohol withdrawal attacks. They are the drugs of choice to arrest status epilepticus of all kinds and eclamptic convulsions. Grand mal, focal and partial (psychomotor, temporal lobe) seizures are less often controlled and grand mal may be aggravated. Because tolerance may develop. The benzodiazepines are most effective when given parenterally and less effective when given continuously by mouth. Toxicity, usually drowsiness or ataxia, is less apt to be troublesome when the dose is increased gradually. 213 references. (Author abstract)

201898 Wheatley, David. no address **Progress in anxiety states.** Proceedings of the Royal Society of Medicine (London). 66(3):255-256, 1973.

The use of the benzodiazepines in the treatment of anxiety is reviewed. A comparison study of chlordiazepoxide with amylobarbitone showed that better results were obtained with the former drug. Sedation studies which compared phenobarbitone with imipramine showed generally the same results. Allaying anxiety symptoms in the milder forms of depression may be more rapidly achieved with antianxiety drugs than with specific antidepressants. Chlordiazepoxide produced better results than propranolol in the treatment of depression and sleep disturbance but no differences in the antianxiety effects of the two drugs were found. Doctor's and patient's attitudes towards the use of chlordiazepoxide is also discussed.

202037 Israel, L.; Merlet, A.; Gault, J.-L.; Klotz, J.-P.; Paul, C.; Poupier, G. no address **/Clinical study of Gerdaxyl 10mg with 40 patients treated in a psychiatric outpatient facility./** Etude clinique du Gerdaxyl 10mg portant sur 40 patients traites en psychiatrie ambulatoire. Information Psychiatrique (Lyon). 50(6):655-657, 1974.

A clinical study of Gerdaxyl was carried out with 40 depressed patients treated in a psychiatric outpatient service. Results were good in 67.5% of the cases, unsatisfactory in 20%, and a failure in 12.5%. Psychotherapy was carried out simultaneously with administration of the drug. Compared to the thymoanaleptic effects of the tricyclic derivatives, the antidepressant action of Gerdaxyl takes longer to take effect. One of the reasons may be insufficient dosage. Gerdaxyl is not indicated for severe depression. Tolerance to the drug is very good.

202069 Quidu, M. Hopital Gourmelen, 29000 Quimper, France **/Interest of sulpiride in kinetic disturbances./** Interet du sulpiride dans les troubles kinetiques. Semaine des Hopitaux Therapeutique (Paris). 50(5-6):397-398, 1974.

The efficacy of sulpiride in treating kinetic disturbances is discussed, illustrated by a case history. The patient under con-

sideration was first diagnosed as suffering from Huntington's chorea, a diagnosis later refuted. It was finally decided that there was neurological symptomatology with extrapyramidal expression which was known to have been present prior to neuroleptic treatment; disturbances in mood (anxiety, depression, irratibility); and the beginning of intellectual deterioration. Administration of sulpiride had a beneficial effect both on neurological symptoms and psychic symptoms. The high dosages used were well tolerated and proved to be effective where other psychotropic drugs had only acted incompletely.

202121 Sasaki, Kuniyuki. Sasaki Hospital, Japan **Ketamine hydrochloride as a preanesthesia drug for an electroshock treatment.** Medical Consultation and New Remedies (Tokyo). 8(4):127-129, 1971.

Ketamine hydrochloride (50 mg intravenously) as a preanesthesia drug for electroshock treatment in a mixed sample of schizophrenic, depressed and neurotic patients was examined. This drug did not induce an increase or decrease in the intensity of convulsion or have any side-effects. Respiration automatically occurred in all the patients 5 to 10 minutes after convulsion, and most of the patients could walk by themselves 30 to 40 minutes after convulsion. No kinetic excitation or delusion was observed after convulsion. This drug is quite useful as a preanesthesia drug for electroshock treatment. 4 references.

202162 Kato, Shin. Shinkei Kenkyusho, Japan **DPAM and cerebral function (second report): psychopharmacological implications.** Igaku no Ayumi (Tokyo). 82(13):799-806, 1972.

The literature on the relationship between dopamine and mental illness and psychopharmacology is reviewed. The relationship of dopamine with Parkinsonism, manic-depression and schizophrenia, and the psychopharmacological mechanism of L-dopa, anticholinergic agents, antihistamine derivatives, central nervous system stimulants, apomorphine and amantadine on Parkinsonism, and of L-dopa and alpha-methyl-Dopa on depression are considered. The relationship between schizophrenia and dopamine is also discussed. 98 references.

202282 Klawans, Harold L.; Weiner, William J. Division of Neurology, Michael Reese Medical Center, 29th and Ellis Ave., Chicago, IL 60616 **The effect of d-amphetamine on choreiform movement disorders.** Neurology. 24(4):312-318, 1974.

The effect of d-amphetamine on choreiform movement disorders was studied. d-Amphetamine was given to patients with Huntington's chorea, Sydenham's chorea, and chorea associated with systemic lupus erythematosus, and to normal volunteers. d-Amphetamine worsened already existing chorea. The drug also elicited chorea in one patient but not in the normal individuals. Since the dopamine antagonist haloperidol blocked this effect d-amphetamine may elicit chorea through a striatal dopaminergic mechanism. The data suggest that altered striatal dopamine sensitivity is a necessary factor in d-amphetamine-induced chorea and that a similar alteration in striatal dopaminergic sensitivity may be present in chronic amphetamine abusers with chorea and paranoid psychoses. 50 references. (Journal abstract modified)

202356 Christensen, Donald Eugene. Univ. of Illinois at Urbana-Champaign **The combined effects of methylphenidate (ritalin) and a classroom behavior modification program in reducing the hyperkinetic behaviors of institutionalized mental retardates. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-Films, No. 74-11981 HC$10.00 MF$4.00 160 p.

The behavioral effects of the psychotropic medication methylphenidate (Ritalin) when administerd in conjunction with a program of behavior therapy were investigated. Sixteen hyperactive, institutionalized mentally-retarded children served as subjects for the 12-week study. Effects of environmental and drug treatment programs were assessed by a variety of dependent measures, including academic performance, teacher ratings, seat activity, and direct observation of classroom behavior. Significant treatment effects were revealed on academic productivity, teacher ratings and 8 of the 12 categories of the observation instrument. Results are interpreted as indicating behavior modification to be a more potent form of treatment than drug therapy for the behavior disorders studied. It is concluded that behavior modification is a viable alternative to drug treatment for children with hyperactive behavior disorders. (Journal abstract modified)

202798 de Groot, M. H. L. Baillie Henderson Hospital, Toowoomba, Queensland, Australia **The clinical use of psychotherapeutic drugs in the elderly.** Drugs (Basel). 8(2):132-138, 1974.

The use of psychotherapeutic drugs in the elderly was examined. It is suggested that they can be of extreme value. It has been shown in a survey in Sydney that of over 200 patients admitted to a psychogeriatric unit, 16% of these admissions were directly attributed to the ill effects of the psychotherapeutic drugs. These ill effects were: 1) simple intoxication; 2) secondary drug effects occurring in association with the mental disturbance (three patients in this group had fractures following falls); and 3) disinhibition reactions, e.g. agitation and aggression. It is concluded that if the rules outlined are followed these troubles can be avoided and the geriatric patient will be helped considerably by the medication. 4 references.

202824 Page, John G.; Janicki, Robert S.; Bernstein, Joel E.; Curran, Charles F.; Michelli, Frank A. Abbott Laboratories, Pharmaceutical Products Division, North Chicago, IL 60064 **Pemoline (Cylert) in the treatment of childhood hyperkinesis.** Journal of Learning Disabilities. 7(8):498-503, 1974.

A controlled, double-blind study using pemoline and placebo in the management of hyperkinetic behavior associated with minimal brain dysfunction is described. Improvement in gross behavior, as measured by parent, teacher and physician global evaluations, as well as improvement in cognitive and perceptual function as measured by psychological tests, is recorded for the pemoline group. This was achieved with minimal side-effects on a once daily dosage regimen, indicating that pemoline is a highly useful clinical alternative to the amphetamines and methylphenidate as an adjunct in the management of hyperkinetic behavior. 7 references. (Author abstract)

203423 Del Portillo, Lorenzo. Central Georgia Regional Hospital Complex, Milledgeville, GA 31062 **Piperacetazine study in state hospital patients.** Journal of the Medical Association of Georgia. 63(12):465-467, 1974.

Piperacetazine therapy was evaluated over a 12-week period in various types of mentally ill patients in a state hospital environment. Improvement was observed in 86% of the 43 patient population studied. Side-effects were minimal. Four patients exhibited tremors which were readily controlled by an antiparkinson agent. Only one patient was discontinued from the project due to drowsiness. Results suggest that piperacetazine therapy may be quite useful in the hospitalized mentally ill patient. 4 references. (Author abstract modified)

203470 Fann, William E.; Wheless, Jeanine C.; Richman, Bruce W. Dept. of Psychiatry, Baylor College of Medicine, 1200 Moursund Ave., Houston, TX 77025 **Psychopharmacological treatment of disorders of senescence.** North Carolina Medical Journal. 35(11):672-677, 1974.

Advantages and detriments of major drug classes used in the treatment of various psychiatric syndromes of the elderly are discussed. Consideration is given to the use of stimulants, vasodilators, hormones, vitamins, anticoagulants, nootropic agents and rejuvenating drugs. The need for accurate treatment and assessment of disorders within this population is discussed, in view of a predisposition toward the diagnosis of senility in psychiatrically-compromised geriatric patients. Elderly patients may present with the entire range of psychopathologic symptoms, in either the absence or presence of actual senile symptomatology. 25 references. (Author abstract modified)

203598 Vyncke, J. Witrand Institution, Potchefstroom, Transavaal, South Africa **The treatment of behavior disorders in idiocy and imbecility with clozapine.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 7(5):225-229, 1974.

The use of clozapine (Leponex) for the treatment of 40 severe, refractory behavior disorders is reported. The preparation was especially effective in imbecilic patients but its efficacy in behavior disorders was not as great. The effect of Leponex on behavior disorders was not seen to be due to its sedative properties, but was ascribed to the compound's thymoleptic properties. The preparation also relieves dysphoria and anxiety, with the side-effects being slight and transient. 13 references. (Author abstract modified)

203606 Eisdorfer, Carl; Fann, William E. Dept. of Psychiatry, Univ. of Washington Medical School, Seattle, WA **Psychopharmacology and aging.** New York, Plenum Press, 1973. 253 p. $12.50.

Current information on the clinical uses and implications of psychoactive agents as they relate to the elderly patient's physical and mental well-being are examined. Unpublished materials are reviewed and the literature is surveyed. The following topics are discussed: the abuse potential of mild analgesics; management of age-related patient are discussed: the abuse potential of age related changes at changes at the tissue level of cyclic AMP; and the utilization of medication in nursing homes.

203742 Teichmann, Helfried; Schwebke, Rainer. Universitats-Nervenkelinik, 25 Rostock 9, Germany /**Performances under Cerutil of normally intelligent children affected by cerebroorganic reductions in efficiency.**/ Die Leistungen hirnorganisch leistungsgeminderter normal-intelligenter Kinder unter Cerutil in Arbeitsversuch. Psychiatrie, Neurologie und medizinsche Psychologie (Leipzig). 25(3):168-177, 1973.

Eighteen normal 10-year-old pupils of the sixth special school for normal pupils affected by cerebroorganic efficiency reductions were tested for the effect of Cerutil (VEB Isis, Zwickau) in the concentrated loading test after Pauli and according to the test plan of a self-controlled alternate repetition. After an administration for 18 days (200mg/day for 7 days; 300mg in the morning and 300mg at noon every day for 11 days) the drug effected a mean decrease in efficiency of 9.9% due to a reduction in the purposeful mental activity, defined by the number of problems present per unit of time in the Pauli test. Since the quality of work done also is debased, a true deterioration in efficiency is given. 16 references. (Journal abstract)

204528 Wright, David Ferrell. University of Southern California **An ecological approach to a behavior disorder: enuresis. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-26059 HC$12.50 MF$4.00 204 p.

The relative effects of two environmental manipulations (pharmacological and behavioral) on the enuretic behavior of subjects from 6- to 13-years-old were examined and the usefulness of an ecological model in such treatment was assessed. Pharmacological treatment involved administration of imipramine. The behavioral approach was based on the proposition that such behavior is acquired and eliminated according to the learning principles that apply to all behaviors and emphasizes the surrounding environment as positive reinforcement for appropriate behavior changes to maintain normal urinary functions. Nine of the 10 subjects who entered the 16-week program achieved complete bladder control. Statistical analyses showed that behavioral intervention was significantly faster in effecting remission than imipramine treatment. Some subjects required imipramine treatment plus behavioral intervention to achieve remission. (Journal abstract modified)

204688 Post, Georgia Rodee. University of Southern California **The differentiation of two types of hyperactive children by activity level and task performance with methylphenidate (Ritalin) and placebo. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-26044 HC$12.50 MF$4.00 350 p.

Two types of male hyperactive children were differentiated by activity level (as measured by a stabilimetric chair) and task performance (as determined by picture recognition, formboard, Porteus Maze, operant conditioning with a differential low rate (DRL) schedule, and directed activity) when treated with methylphenidate (Ritalin) and a placebo. Statistical analyses of data reveal that four variables were highly correlated with clinical recommendations for Ritalin: placebo activity levels during the difficult picture recognition task, placebo activity levels during the DRL operant task, placebo performance on the directed activity task, and placebo performance on the DRL operant task. Significant differences were also noted for a number of activity measures. The drug significantly reduced the resting activity and total activity of the recommended subjects, who were more active than the nonrecommended Ss in overall activity. (Journal abstract modified)

205031 Rodin, E. A.; Rim, C. S.; Rennick, P. M. Lafayette Clinic, 951 East Lafayette, Detroit, MI 48207 **The effects of carbamazepine on patients with psychomotor epilepsy: results of a double-blind study.** Epilepsia (Amsterdam). 15(4):547-561, 1974.

A double-blind study of the anticonvulsant and psychotropic properties of carbamazepine (Tegretol) was made with 37 hospitalized patients with intractable psychomotor epilepsy. Patients were first stabilized on diphenylhydantoin and phenobarbital and then received for two 3-week periods identical capsules containing either carbamazepine first, then placebo, or vice versa. Telemetric EEGs were recorded during each period and routine EEGs weekly; routine laboratory tests were also performed. Carbemazepine reduced the frequency of psychomotor seizures by 83%, and reduced grand mal seizures by 55%. Side-effects were minor; behavioral effects were not demonstrable on a double-blind basis. The drug tended to produce slowing of background EEG rhythms and sometimes diffuse paroxysmal activity; temporal spikes could diminish and be replaced by slow waves or they could increase. It is

concluded that carbamazepine is effective for treatment of psychomotor epilepsy and is safe when blood and platelet counts are checked. 17 references. (Author abstract)

205316 Malcolm, M. T.; Madden, J. S.; Williams, A. E. West Cheshire Hospital, Liverpool Road, Chester, CH1 3ST England **Disulfiram implantation critically evaluated.** British Journal of Psychiatry (London). 125:485-489, 1974.

Sixty-two alcoholic patients were treated by disulfiram implantation to clarify the nature of any deterrent effect of the implant. At followup only three patients described any reaction on drinking and their symptoms were hypothesized to be psychogenic. Blood disulfiram levels above 0.1mg were invariably found after oral disulfiram therapy. Such levels were occasionally recorded after implant, but only during the first postoperative week, when patients were still in the hospital. Carbon disulphide, a metabolite of disulfiram, was measurable in the exhaled breath of patients given oral disulfiram, but, with the exception of one patient, this was not so after implantation. It is believed that implantation does not give alcoholic patients pharmacologically active disulfiram cover, and that the deterrent effect of the procedure is psychological. 18 references. (Author abstract modified)

12 PSYCHOTOMIMETIC EVALUATION STUDIES

198230 Kaplan, J.; Mandel, L. R.; Stillman, R.; Walker, R. W.; VandenHeuvel, W. J. A.; Gillin, J. C.; Wyatt, R. J. Lab. of Clinical Psychopharmacology, Div. of Spec. Mental Health Research, IRP, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Blood and urine levels of N,N-dimethyltryptamine following administration of psychoactive dosages to human subjects.** Psychopharmacologia (Berlin). 38(3):239-245, 1974.

Psychoactive doses (0.7mg/kg) of the hallucinogen N,N-dimethyltryptamine (DMT) were administered intramuscularly to 11 normal subjects. A gas chromatographic-mass spectrometric isotope dilution determination of DMT concentrations in whole blood and urine revealed that only a fraction of the injected dose was recovered and the blood DMT concentrations had a very similar time course to the subjectively-reported "high". 21 references. (Author abstract)

202720 Jarbe, Torbjorn U. C.; Henriksson, Bengt G. University of Uppsala, Department of Psychology, Slottsgrand 3, S-752 20 Uppsala, Sweden **Discriminative response control produced with hashish, tetrahydrocannabinols (delta8-THC and delta9-THC), and other drugs.** Psychopharmacologia (Berlin). 40(1):1-16, 1974.

The discriminative properties of hashish and its derivatives and other noncannabinoid drugs were examined. To determine the specificity of the drug-induced response control, a variety of psychotropic drugs were tested for their possible generalization to the training drugs. It is concluded that tetrahydrocannabinols (THC) are interchangeable with respect to cue function and that hashish, inhaled as smoke, produces cue effects similar to synthetic THC in rats. Neither cannabidiol nor cannabinol evidenced transfer to hashish or its derivatives. Lack of generalization to THC was also apparent for central nervous system (CNS) depressants, anticholinergics, tacrine, sernylan, psilocybine, morphine, CNS stimulants, yohimbine, and phenitrone. Some of these drugs as well as levallorphan tartrate were tested for antagonistic effects but found ineffective in preventing the THC discrimination. Except for atropine, the transfer testings for the noncannabinoid drugs yielded results that were anticipated from previous literature. For example, chlordiazepoxide showed transfer to diazepam. 58 references. (Author abstract modified)

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

198101 Tecce, Joseph J. Boston State Hospital, Dorchester, MA **Psychotropic drugs and slow potentials in man.** Psychopharmacology Bulletin. 10(2):68-69, 1974.

The slow potential of the brain for normal persons who are given psychoactive drugs and then distracted and aroused by different experimental tasks is being studied. The subjects are given a stimulant, a tranquilizer, or a placebo; the resulting changes in their brain waves, heartrate, and muscle tension are recorded. In the first hour postdrug, about half the normal subjects tested showed signs of drowsiness and fatigue, which was accompanied by contingent negative variation (CNV) reduction and decreased levels of heartrate. In the second and third hours postdrug, these "paradoxical" subjects, as well as others, showed signs of alertness and narrowed attention. During this time, CNV amplitude was enhanced and heartrate levels were elevated. Findings support an attention-arousal model of CNV-behavior associations. (Journal abstract modified)

199519 Stambaugh, John E.; Wainer, Irving W. Department of Pharmacology, Jefferson Medical College of Thomas Jefferson University, Philadelphia, PA 19107 **The bioavailability of meperidine.** Journal of Clinical Pharmacology. 14(10):552-559, 1974.

Pharmacokinetic studies of meperidine are reported, and a highly sensitive gas liquid chromatographic (GLC) technique for the quantification of meperidine in blood serum is described which made it possible to measure serum levels of meperidine following a single 50mg intramuscular injection. The results of a two-way crossover trial of two commerical preparations of meperidine hydrochloride in 24 healthy volunteers is reported. The serum levels of meperidine were followed for a 24-hr period, and serum concentrations as low as 0.01 microgram/ml were detected by GLC. The meperidine serum levels resulting from the 50mg doses decreased at a rate of 17.7% per hour with a biologic half life of 3.65 hours, correlating well with the previously reported data of an average clearance of 17% and a biologic half life of 3 to 4 hours. The data showed no statistically significant difference between the serum levels produced from the two preparations, and the preparations are of comparable bioavailability. 8 references. (Author abstract modified)

199621 Bodin, N.-O.; Borg, K. O.; Johansson, R.; Obianwu, H.; Svensson, R. AB Hassle, Fack, S-431 20 Molndal, Sweden **Absorption, distribution and excretion of alprenolol in man, dog, and rat.** Acta Pharmacologica et Toxicologica (Copenhagen). 35(4):261-269, 1974.

The plasma levels of unchanged alprenolol and its radioactive metabolites were determined in four healthy male volunteers after intravenous and oral administration of 3H-alprenolol. In the rat the tissue distribution was studied after intravenous and oral administration by determination of unchanged drug and its radioactive metabolites in eight different tissues. A high degree of extravascular distribution of the drug was observed, with especially high amounts of unchanged alprenolol in the lung after intravenous administration. In the rat, dog, and man the urinary excretion of total radioactivity after intravenous and oral administration of 3H-alprenolol was studied, and the drug was completely absorbed after oral administration. In man the drug was almost completely excreted in the urine within 48 hours mainly as metabolites. In the rat and dog a considerable amount was

excreted in the feces. From studies in the rat and dog it was demonstrated that this was due to biliary excretion of the drug. 13 references. (Author abstract modified)

199756 Frost, J. D., Jr.; Carrie, J. R. G.; Borda, R. P.; Kellaway, P. Neurophysiology Department, Methodist Hospital, Houston, TX 77025 **The effects of Dalmane (flurazepam hydrochloride) on human EEG characteristics.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(2):171-175, 1973.

The changes that occurred in the waking electroencephalograms (EEG) of six normal subjects during the oral administration of flurazepam hydrochloride (Dalmane) were evaluated. Some of these changes were examined quantitatively with the use of a computer analysis technique. While the subjects were receiving the drug, there was an increase in the amount of beta activity. This increase in beta activity was maximal in frontocentral leads and was characterized by an increase in the number of waves that occurred during an EEG recording interval of fixed duration, with no consistent change in mean EEG wave length (frequency) or average wave amplitude within the beta frequency range. EEG activity in the central occipital leads showed a reduction in the frequency of occurrence of waves in the alpha (6-14 c/sec) and theta (3-7 c/sec) ranges during flurazepam administration. 17 references. (Author abstract modified)

199757 Guilleminault, C.; Cathala, J. P.; Castaigne, P. Department of Psychiatry, Stanford University School of Medicine, Stanford, CA 94305 **Effects of 5-hydroxytryptophan on sleep of a patient with a brain-stem lesion.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(2):177-184, 1973.

The sleep of a young adult male suffering from hyposomnia following a car accident 6 years ago was studied with the aid of polygraphic recording. The clinical examination found neurological sequels, which showed, among other things, a brainstem lesion with a third cranial nerve impairment. The lumbar puncture showed an abnormally low level of 5-hydroxyindoleacetic acid in the cerebrospinal fluid. The effects on sleep in this patient of 5-hydroxtryptophan (5HTP), precursor of serotonin, have been studied with polygraphic recording. Two different types of results were observed which may be associated with different doses of 5HTP and the diverse possibilities of metabolic transformation of the precursor. 26 references. (Author abstract modified)

199782 Scott, D. F.; Schwartz, M. S.; Farrant, G. W.; Speirs, C. F. EEG Department, London Hospital, London E.1, England **The importance of methodology in drug studies using EEG.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 37(6):670-672, 1974.

The importance the methodology in drug studies using the electroencephalogram (EEG) was examined. The EEG has proved of value for the objective assessment of psychoactive drugs especially when studied in association with other measures such as blood levels of the compound or behavioral testing. When the drug being investigated gives rise to drowsiness and sleep, strict methodology is particularly important because of a strong tendency for subjects to become less alert with repeated EEGs. During a double-blind investigation of a new adamanatane compound for its possible central nervous depressant effects, the eight normal volunteer subjects all showed more marked drowsiness and sleep in the second recording as compared with the first. The second tracing was almost always regarded as the more abnormal. However, as a strictly balanced design with placebo control was employed it was possible to show that these EEG changes were not the result of drug administration but an order effect. 11 references. (Author abstract)

199913 Gauch, R.; Modestin, J. Forschungsinstitut der Wander AG, Bern, Switzerland **/On the pharmacokinetics of dibenzepine./** Zur pharmakokinetik von dibenzepin. Arzneimittel-Forschung (Aulendorf). 23(5):687-690, 1974.

In a pharmacokinetic study, 12 female patients with endogenous depressions were treated with dibenzepine (8mg/kg body weight) for a minimum of 22 days. It was found that the dibenzepine was rapidly absorbed from the tablets and was rapidly metabolized. Elimination of the drug and its metabolites was also rapid (t1/2 4 hr). In addition to the dibenzepine itself, the monodesmethyl derivative demethylated in the side chain was found to be the principal metabolite in the plasma of all patients. A steady state was not attained with normal doses. The plasma concentration of dibenzepine declined slightly during therapy on a fixed dosage. There was a positive correlation between the patients' age and the combined plasma level of dibenzepine and the demethylated side chain metabolite. 11 references (Author abstract modified)

200049 Ballinger, B. R.; Presley, A.; Reid, A. H.; Stevenson, I. H. Royal Dundee Liff Hospital, University of Dundee, Dundee, Scotland **The effects of hypnotics on imipramine treatment.** Psychopharmacologia (Berlin). 39(3):267-274, 1974.

Plasma imipramine (IMI) and desmethylimipramine concentrations and depression ratings were measured over a 3-week period in three groups of hospitalized depressed patients given standard doses of imipramine. The first group received imipramine alone, the others either amylobarbitone or nitrazepam in addition as a night sedative. The plasma antidepressant levels were consistently higher in the group receiving no hypnotic but only significantly so in the case of total IMI in the imipramine alone group compared to the group receiving imipramine plus amylobarbitone. The interindividual differences in plasma levels were large. There was no difference between the groups with regard to changes in depression, sleep or side-effects. 14 references. (Author abstract modified)

200071 Solovyev, L. A. Leningrad Scientific Experimental Neuropsychiatric Institute, Leniningrad, USSR **/The sparing technique in electroconvulsive therapy./** K voprosu o shchadyashchey metodike elektrosudorozhnoy terapii. Zhurnal Nevropatologii i Psikhiatrii Imeni S. S. Korsakova (Moskva). 74(7):1046-1052, 1974.

Methods of avoiding side-effects and complications which accompany electroconvulsive therapy (ECT) were studied. Mild tranquilizers (fenibut and seduxen) which do not significantly influence the threshold of convulsive readiness were administered prior to ECT to 112 patients. It was found that the use of fenibut and seduxen reduced the duration of respiratory retardation, prevents or reduces postseizure excitation, and obliterates or prevents anamnestic disorders. The drugs did not influence the therapeutic effect. Use of sparing ECT procedures is especially indicated in patients where treatment may elicit side-effects, particularly in older patients. 19 references. (Journal abstract)

200086 Klawans, H. L.; Rubovits, R. Division of Neurology, Michael Reese Medical Center, Chicago, IL 60616 **Effect of cholinergic and anticholinergic agents on tardive dyskinesia.** Journal of Neurology, Neurosurgery, and Psychiatry (London). 27(8):941-947, 1974.

The effects of cholinergic and anticholinergic agents on tardive dyskinesia which is thought to be primarily related to dopaminergic activity within the striatum were studied. Physostigmine has been demonstrated to improve the abnormal movements in patients with tardive dyskinesia while scopolamine tends to aggravate abnormal movements and in some cases elicits abnormal movement not previously observed. This evidence supports the hypothesis that anticholinergic therapy in patients prone to develop tardive dyskinesia may increase the incidence of this disorder by lowering the threshold for the appearance of these movements. 23 references. (Author abstract modified)

200773 Domino, Edward F.; Krause, Rachel R. Michigan Neuropsychopharmacology Research Program, Laboratory of Pharmacology, Lafayette Clinic, Detroit, MI 48207 **Plasma tryptophan tolerance curves in drug-free normal controls, schizophrenic patients and prisoner volunteers.** Journal of Psychiatric Research (Oxford). 10(3&4):247-161, 1974.

Plasma tryptophan (TP) was determined fluorometrically in four groups of males: (1) normal controls (2) chronic schizophrenics (3) acute schizophrenics and (4) prison volunteers with personality disorders with and without symptoms of depression. Fasting a.m. or p.m. plasma TP was within the range of normal for all groups. However, the acute schizophrenics and prison volunteers had lower plasma TP than the normal controls and chronic schizophrenics. Plasma TP was determined before an 8.00 a.m. TP load and at .5, 1, 2, 4 and 7 hr after ingestion. A plasma tolerance curve was obtained with a peak at 1-2 hr which returned almost to normal at 7 hr. Various TP parameters were measured. Almost no significant differences were found between normal controls and the chronic schizophrenics. Although all prison volunteers showed a markedly different TP tolerance curve from either the normal controls or chronic schizohprenics, depressed prisoners had a significantly lower and flatter curve. It appears that TP is well absorbed from the gastronintestinal tract and its plasma half-life is normal in chronic schziophrenics. 52 references. (Author abstract modified)

201327 El-Yousef, M. Khaled. Tennessee Neuropsychiatric Institute, 1501 Murfreesboro Road, Nashville, TN 37217 **Effects of conjugated estrogens on plasma butaperazine levels.** Psychopharmacologia (Berlin). 39(1):39-41, 1974.

A randomly-assigned control experimental grouping with a crossover design, using subjects as their own controls, was utilized to study the effects of conjugated estrogens on plasma butaperazine (Repoise) levels in postmenopausal female subjects. Significantly higher plasma butaperazine levels were measured following both a single loading dose and with maintenance doses of oral butaperazine in subjects when they were taking conjugated estrogens as compared to when they were not taking conjugated estrogens. The underlying mechanisms for these findings and their clinical implications are discussed. 7 references. (Author abstract)

201328 Lagergren, Krister; Levander, Sten. Department of Psychiatry, Karolinska sjukhuset, S-104 01, Stockholm 60, Sweden **A double-blind study on the effects of Piracetam upon perceptual and psychomotor performance at varied heart rates in patients treated with artificial pacemakers.** Psychopharmacologia (Berlin). 39(1):97-104, 1974.

Twelve patients treated with artificial pacemakers were given 1.6g Piracetam per os three times daily for 9 days and placebo for another 9 days. The effects on performance were compared in critical flicker fusion (CFF), reaction time (RT), and vernier visual acuity (KVAT), at heartrate of 70 and 45 beats/min in sitting position. With placebo there were significant impairments in CFF and RT at 45 beats/min and a similar trend in KVAT. With Piracetam there were significantly less impairments in CFF at 45 beats/min and similar trends in RT and KVAT. With Piracetam there were also significant increases in KVAT, irrespective of heartrate, compared with placebo. With regard to the differences in circulatory dynamics between 70 and 45 beats/min, the results indicate that Piracetam had some protective effect against the influence of an assumed cerebral hypoxia at the lower rate or a cortical arousing effect, which counteracted the decrement in vigilance associated with the slow heartrate. 22 references. (Author abstract modified)

202194 Collier, H. O. J. Research Division, Miles Laboratories Limited, Stoke Poges, Slough, Bucks, England **The concept of the quasi-abstinence effect and its use in the investigation of dependence mechanisms.** Pharmacology (Basel). 11(1):58-61,1974.

The question of whether dependence mechanisms can be investigated by scrutinizing positively-induced 'quasiabstinence' effects is discussed. Possible inducers of such effects such as 5-hydroxytryptophan and theophylline are examined. 10 references. (Author abstract)

202307 Mendelson, Jack H.; Mello, Nancy K. Harvard Medical School, Boston, MA 02115 **Plasma testosterone levels during chronic heroin use and protracted abstinence.** Pharmacologist. 16(2):193, 1974.

At the fall metting of the American Society for Pharmacology and Experimental Therapeutics, the effects of heroin on plasma testosterone (T) levels in Hong Kong heroin addicts was undertaken. The mean T level for six adult males between the ages of 23 and 43 determined within 4 to 5 hours following last intravenous dose of heroin was 227ng/100 ml. Three subjects with abstinence of 1 month or less had T levels which were not significantly different from those subjects who were actively using heroin. However, 15 subjects who were abstinent over 1 month to 1 year had T values which were significantly higher than those subjects who were using heroin. These data indicate that chronic heroin use may be associated with suppression plasma T levels but that T levels return to normal following protracted abstinence. (Author abstract modified)

202699 Braithwaite, R. A.; Nakra, B. R. S.; Gaind, R. Poisons Unit, Guy's Hospital, London SE1, England **Steady-state plasma concentrations during single and multiple dosage schedules of amitriptyline**. Psychological Medicine (London). 4(3):338-341, 1974.

Plasma amitriptyline and nortriptyline concentrations were measured in a group of five adult subjects who each received two different dosage regimes of amitriptyline (Tryptizol) for 14-day periods (namely, 25mg three times daily and 75mg once nightly). Mean steady state plasma concentrations during the two dosage regimes were in close accord. The daily variation in drug plasma concentrations were only minimal during the thrice daily dosage regime but during the once nightly dosage regime there was an average decline in total drug plasma concentrations (amitriptyline plus nortriptyline) of about 30%. It was concluded that antidepressant medication with amitriptyline using a single nightly dose schedule might be more reliably taken by patients without any significant reduction in therapeutic efficacy. 17 references. (Author abstract)

202925 Lyubchenko, P. N.; Drozdova, G. A.; Borodulina, O. V.; Boyarchuk, Z. I.; Turayev, R. N.; Dubova, V. G. Oblastnoy klinicheskiy institut im. M. F. Bladimirskogo, U.S.S.R. **/Liver function in workers occupationally dealing with chlorpromazine and some other compounds./** Funktsional0noye sostoyaniye pecheni u rabochikh imeyushchikh proizvodstvennyy kontakt s aminazinom i nekotorymi drugimi soyedineniyami. Gigiyena Truda i Professional0nyye Zabolevaniya (Moscow). No. 9:47-48, 1974.

The effect of exposure to chlorpromazine, hexachlorine and carbon tetrachloride (CC14) on the liver was investigated in three groups of workers. Eighteen of the participants worked in a chlorpromazine pharmaceutical factory, where chlorpromazine dust concentration was very high; 18 worked in the oxygen department, where their contact with CC14 was sporadic; 27 worked in the chemical weed killer division, where hexachlorine concentration was unusually high. All participants had been working for 4 to 20 years. All three compounds, in various concentrations, were found to elicit identical light displacements in cholinesterase activity, as well as deterioration in the excretory function of the liver. Chlorpromazine caused moderate decline in tyrosine content level in the blood. CC14 caused an increase in amino acids in the blood stream. 7 references.

202966 Calvert, A.; Mitchell, A. S.; Sinclair, G. Sydney Hospital, Macquarie Street, Sydney, New South Wales 2000, Australia **A double-blind evaluation of diazepam and amylobarbitone in acute myocardial infarction.** Medical Journal of Australia (Sydney). 2(17):624-627, 1974.

A double-blind trial of two sedatives, amylobarbitone and diazepam, was performed in 215 consecutive patients with acute myocardial infarction. Assessment was made of their relative effectiveness as sedatives, and of their influence on the clinical course of the patients. Patients receiving amylobarbitone showed a greater incidence of adverse response to sedation. This difference was significant, and was due to more variable response to a fixed dosage of the drug. The clinical course and outcome in the two groups were similar. In those patients who tolerated the sedation, no difference between the two sedatives was seen, in either the incidence of adverse psychological responses, or in repeated psychological testing. (Author abstract)

203005 Greenblatt, David J.; Shader, Richard I.; Koch-Weser, Jan. Massachusetts General Hospital, Boston, MA 02114 **Pharmacokinetic determinants of the response to single doses of chlordiazepoxide.** American Journal of Psychiatry 131(12):1395-1397, 1974.

Pharmacokinetic determinants of the response to single doses of chlordiazepoxide were investigated. Blood concentrations of this minor tranquilizer were measured in nine healthy volunteers after administration of single 25mg doses. Peak blood concentrations and rates of absorption and disappearance varied considerably among the subjects. Such pharmacokinetic variations have important clinical consequences and probably contribute to individual differences in the response to minor tranquilizers. 10 references. (Author abstract modified)

203645 Schulz, Manfred; Grimm, Ulrich; Schmitz, Willi; Knapp, Alwin. 212 Ueckermunde, Robert-Koch-Strasse, Germany **/Tryptophan metabolism examinations in oligophrenic children. First report: Results of the excretion of kynurenine and xanthurenic acid after tryptophan loading and their dependence upon the supply/** Tryptophanstoffwechseluntersuchungen bei oligophrenen Kindern. 1. Mitteilung: Ergebnisse der Kynurenin- und Xanthurensaureausscheidung nach Tryptophanbelastung und deren Abhangigkeit von der Vitamin B6-Zufuhr. Psychiatrie, Neurologie und medizinische Psychologie (Leipzig). 25(2):98-106, 1973.

The excretion of kynurenine and xanthurenic acid after tryptophan loading was examined in oligophrenic children and the dependence of this metabolic process on vitamin-B6 was examined. Eighty-one children were examined after tryptophan loading and the excretion of xanthurenic acid and kynurenine in the urine passed in 24 hours was tested. With 60% of the children the test was positive, with 16% slightly positive; 31% of the largely positive children were premedicated with high doses of vitamin-B6 and then subjected to another tryptophan test. Thereafter, the excretion of xanthurenic acid and kynurenine was reduced or normalized significantly in children where hereditary oligophrenia was present, whereas in children with brain damage contracted in their infancy little or no significant reduction of the excretion of xanthurenic acid and kynurenine was observed. 15 references. (Journal abstract)

203701 Gottschalk, Helga; Sack, Gerhard. EEG Abteilung des Fachbereiches Neurologie/Psychiatrie der Karl-Marx-Universitat Leipzig, DDR-701, Emilienstrasse 30, Germany **/EEG examinations during lithium treatment./** EEG-Untersuchungen unter Lithiumbehandlung. Psychiatrie, Neurologie und medizinische Psychologie (Leipzig). 25(5):297-300, 1973.

The EEGs of 17 patients before stabilization to lithium and after an average of 5 months were examined. The percentage of pathological findings increased overall and frequently an activation of very slight EEG changes during treatment occurred. Intermittent functional disturbances were common. A relationship between the degree of EEG changes and the lithium level in the serum could not be determined. 10 references. (Journal abstract modified)

203839 Helmchen, H.; Hippius, H. Psychiatrische Klinik II der Freien Universitat Berlin, 1 Berlin 19, Nussbaumallee 36, Germany **/Multidimensional psychopharmacotherapeutic trials with the neuroleptic Perazine. 1. Communication: setting a goal and methodological ground rules./** Multidimensionale pharmakopsychiatrische Untersuchungen mit dem Neuroleptikum Perazin. 1. Mitteilung: Zielsetzung und methodische Grundlagen. Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 7(1):1-8, 1974.

A multidimensional pharmacopsychiatric study of 60 patients with the neuroleptic drug Perazine is described. The course of illness was documented by the AMP-System, an instrument which is in common use in German-speaking countries, to describe and measure psychopathological findings: serum concentrations of Perazine; serum concentration of sodium, potassium and calcium; complete hemogram; urine status; electroencephalogram; electrocardiogram; handwriting as a criterion for subtle changes in extrapyramidal movements; and the adjective checklist according to Zerssen. 23 references. (Author abstract modified)

203841 Hadass, H.; Hippius, H.; Mauruschat, W.; Muller-Oerlinghausen, B.; Rosenberg, L. no address **/Multidimensional psychopharmacotherapeutic trials with the neuroleptic perazine. 3rd. Communication: Perazine concentration in blood and clinical efficacy./** Multidimensionale pharmakopsychiatrische Untersuchungen mit dem Neuroleptikum Perazin. 3. Mitteilung: Perazin-Konzentration im Blut und klinisches Wirkungsbild. Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 7(1):17-30, 1974.

A 30-day drug study of the neuroleptic perazine with 48 patients is reported. Blood concentrations of perazine were determined six times during the 30 days of treatment. Blood levels as well as the maximal values differed widely between individuals. No correlation between blood levels of the drug and the kind of disease, sex or age of the patients could be established. The blood concentrations were not dependent on the applied doses/kg bodyweight. Frequency and onset of remission of psychotic symptoms did not correlate with drug concentrations in the blood. 36 references. (Author abstract modified)

203842 Helmchen, H.; Kanowski, S.; Rosenberg, L. Psychiatrische Klinik II der Freien Universitat Berlin, 1 Berlin 19, Nussbaumallee 36, Germany /**Multidimensional psychopharmacotherapeutic trials with the neuroleptic Perazine. 4. Communication: Connection between EEG changes, concentration in blood, and other clinical variables.**/ Multidimensionale pharmakopsychiatrische Untersuchungen mit dem Neuroleptikum Perazin. 4. Mitteilung: Beziehungen zwischen EEG-Veranderungen, Perazin-Konzentration im Blut und anderen klinischen Variablen. Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 7(1):31-41, 1974.

Perazine was administered to 40 patients (20 men and 20 women), and correlations were sought between values for electroencephalograms, blood concentration of psychotropic drugs and psychopathological findings. No correlations were found. Results show that sex must be taken into consideration in the analyses. There are correlations between the manifestation of temporobasal dysrhythmia, paroxysmal dysrhythmia, focal disturbances and the blood concentration, and temporobasal dysrhythmia, paroxysmal dysrhythmia and intermittent slow monorhythmic activity are related to clinical improvement. 31 references. (Author abstract modified)

203843 Malin, J.-P.; Rosenberg, L. Neurochirurg.-Neurol. Klinik der Freien Universitat Berlin, Klinikum Westend, 1 Berlin 19, Spandauer Damm 130, Berlin /**Multidimensional psychopharmacotherapeutic trials with the neuroleptic Perazine. 5. Communication: Influence on ventricular excitation in the electrocardiogram.**/ Multidimensionale pharmakopsychiatrische Untersuchungen mit dem Neuroleptikum Perazin. 5. Mitteilung: Beeinflussung der vertrikularen Erregungsruckbildung im Elektrokardiogramm. Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 7(1):42-49, 1974.

A 30-day treatment of 31 patients with Perazine in which the electrocardiogram was also investigated is reported. After treatment, the amplitude of the T-wave and the plane under the T-waves was smaller in both the male and female subjects. Females showed the effect earlier than men did. For both male and female patients, an undulatory course of disturbances of excitation decrease was registered. Blood pressures in both males and females was significantly lowered by Perazine treatment. Values for diastolic pressure were lowered earlier than values of systolic pressure. The effect on blood pressure is more intense for women than for men and reaches a maximum in both on the 30th day of treatment. Since women were about 15 years older than the male patients, it could not be determined whether effects were due to age or sex. 20 references. (Author abstract modified)

203844 Renfordt, E.; Rosenberg, L. Psychiatrische Klinik II der Freien Universitat Berlin, 1 Berlin 19, Nussbaumallee 36, Germany /**Multidimensional psychopharmacotherapeutic trials with the neuroleptic Perazine. 6. Communication: Relationship between neuroleptic hypokinesis and antipsychotic therapeutic results.**/ Multidimensionale pharmakopsychiatrische Untersuchungen mit dem Neuroleptikum Perazin. 6. Mitteilung: Beziehungen zwischen neuroleptischer Hypokinese und antipsychotischem Therapieerfolg. Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 7(1):50-58, 1974.

The hypokinetic extrapyramidal motor disturbances caused by neuroleptics and measured by handwriting analysis are reported. For 30 days a group of 26 psychotic subjects were treated with Perazine and daily samples of handwriting were taken. Planimetrical analysis of the handwriting specimen is the basis used to distinguish various groups of different intensity of hypokinetic reactivity. The differences between the groups were significant. Patients with a more distinct hypokinesia had a better remission of their psychopathological symptomatology. 22 references. (Author abstract modified)

204393 Greil, W.; Schnelle, K.; Seibold, S. Psychiatrische Klinik der Universitat Munchen, 8000 Munchen 2, Nussbaumstrasse 7, Germany /**Intra-extracellular lithium ratio: clinical and experimental findings on thrombocytes and erythrocytes.**/ Intra/extra-zellulares Lithium-Verhaltnis: klinische und experimentelle Befunde an Thrombozyten und Erythrozyten. Arzneimittel-Forschung (Aulendorf). 24(8):1079-1084, 1974.

Three aspects of intracellular/extracellular lithium ratio in thrombocytes and erythrocytes were studied. The effect of lithium on platelet aggregation is a function of intracellular/extracellular lithium content. The intracellular/extracellular ratio of lithium in patients varies widely interindividually, whereas variations within one individual are very small. The pharmacokinetic profiles of lithium acetate and aspartate follow the same compartmental distribution when given intravenously. When given orally, the absorption of acetate was rapid and rather complete but the aspartate was absorbed slowly and only as a fraction of the dose administered. Lithium aspartate has no specific affinity to the intracellular space; the aspartate lacks a specific cation carrier function for lithium. 9 references. (Journal abstract)

204394 Janzik, H.-H.; Heller, S. Neurologische Klinik der Universitat Tubingen, 74 Tubingen, Liebermeisterstr. 18, Germany /**The serum gonadotropin level under the medication of L-Dopa.**/ Der Serum-Gonadotropin-Spiegel unter der Medikation mit L-Dopa. Arzneimittel-Forschung (Aulendorf). 24(8):1084-1085, 1974.

In a study of the serum gonadotropin level, seven Parkinson patients between 60 and 70 years old were administered L-dopa in individual dosages. Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) plasma levels were determined before and during treatment; no significant difference was noted. Three young males between 20 and 25 years old were administered 25-50mg L-dopa intravenously, and FSH and LH levels were determined before and subsequent to medication at fixed intervals. Contrary to expectations, no immediate increase was noted. 8 references. (Journal abstract modified)

204398 Kanig, K. Abt. fur Neurochemie der Universitats-Nervenklinik, 665 Homburg/Saar, Germany /**The influence of encephalotropic drugs on nucleic acid metabolism in the brain.**/ Zum Einfluss enzephalotroper Pharmaka auf den Nukleinsaurestoffwechsel des Gehirns. Arzneimittel-Forschung (Aulendorf). 24(8):1093-1095, 1974.

The role of nucleic acid and protein metabolism in the brain functions, as well as their correlations with the neurotransmitter substances are discussed. The literature data of earlier experiments concerning the nucleic acid metabolism of

psychotics are reported. Bibliographic data about the effect of encephalotropic drugs on the nucleic acid and protein metabolism are enumerated. The influence of pentobarbital, pyritinol and naftidrofuryl on the turnover of RNA, rRNA, and tRNA, respectively, is also demonstrated and discussed. 32 references. (Journal abstract modified)

204402 Zlatnikova, Jana; Consbruch, U.; Degkwitz, R.; Hampel, R. Psych. und Nervenklinik der Universitat, 78 Freiburg, Hauptstr. 5, Germany /**Effect of amitriptyline in long-term autoexperiments: psychophysiologic study and duration of excretion.**/ Uber die Wirkung von Amitriptylin in langfristigen Selbstversuchen: Psychophysiologiche Untersuchungen und Dauer der Ausscheidung. Arzneimittel-Forschung (Aulendorf). 24(8):1103-1106, 1974.

In order to evaluate the effects of amitriptyline in normal subjects, nine healthy subjects were treated with a therapeutic dose of 150mg daily for 4 weeks. Four subjects received only placebos, serving as controls. To further eliminate placebo effects of the drug, all subjects treated with amitriptyline received placebo during the first 2 weeks, and at the end of treatment. During the test period the excretion of free and conjugated, or glucuronated, amitriptyline with the urine was measured. The effects of amitriptyline on psychic parameters were evaluated with the aid of psychological tests. Further autonomic nervous system functions were also studied, and test results were processed by an analysis of variance. There was a considerable variability of values within and between subjects and between the different weeks of the study. The placebo group showed a short-phased course of changes, but the drug group showed a long-phased effect. No consistent effect of amitriptyline was shown. 9 references. (Journal abstract modified)

204414 Eben, E.; Ackenheil, M.; Raese, J.; Ruther, Eckart. Psychiatrische Klinik der Universitat, 8 Munchen 2, Nussbaumstr. 7, Germany /**Biochemical mechanisms of extrapyramidal motoric action of haloperidol in man.**/ Biochemische Mechanismen der extrapyramidalmotorischen Wirkung von Haloperidol am Menschen. Arzneimittel-Forschung (Aulendorf). 24(8):1133-1135, 1974.

Before and 15 days after haloperidol treatment, homovanillic acid (HVA), 3-methoxy-4-hydroxyphenylglycol (MHPG), and 5-hydroxyindoleacetic acid (5-HIAA) were estimated in cerebrospinal fluid (CSF) and urine of 11 inpatients with paranoid hallucinatory syndrome. Psychopathological and extrapyramidal symptoms were also tested. After treatment, HVA in CSF was increased by about 70%, and the ratio HVA/5-HIAA was decreased. The other biochemical parameters were unchanged. No correlation was found between the clear improvement of psychopathological symptoms, the developed extrapyramidal side-effects and biochemical parameters. The results may reflect temporally different reactions of separate biochemical and anatomical systems. 16 references. (Journal abstract modified)

205042 Lehmann, K. Med. Akademie Carl Gustav Carus, Institut fur Pharmakologie und Toxikologie, DDR-801 Dresden, East Germany /**The kinetics of lithium in the human organism.**/ Die Kinetik des Lithiums in menschlichen Organismus. Intern. J. of Clinical Pharmacology, Therapy and Toxicology (Munchen). 10(4):283-291, 1974.

Lithium kinetics were ascertained continuously and comprehensively in healthy male volunteers (aged 21-28). Lithium kinetics follow the law of a two-compartment system. The rate of excretion in healthy test subjects was determined by the back flow from the tissues. Possible participation of active transport processes in the movement of lithium through the organism is discussed. Lithium salts with varying anions do not differ from one another as regards elimination. Only the absorption phase is influenced by the physicochemical differences (solubility). Suggestions are offered concerning preventive measures and therapy with lithium. 31 references. (Journal abstract)

205043 Lehmann, K.; Merten, K. Med. Akademie Carl Gustav Carus, Institut fur Pharmakologie und Toxikologie, DDR-801 Dresden, East Germany /**Elimination of lithium dependent on age in healthy people and patients suffering from renal insufficiency.**/ Die Elimination von Lithium in Abhangigkeit vom Lebensalter bei Gesunden und Niereninsuffizienten. Intern. J. of Clinical Pharmacology, Therapy and Toxicology (Munchen). 10(4):292-298, 1974.

Lithium clearance was ascertained in three groups of test subjects and patients, ascertaining for the first time an exact, describable change in the lithium clearance, dependent on age and renal function of the subjects. Both the serum level curve and the kinetic parameters were changed even after the first oral lithium dose in patients with renal insufficiency. Factors capable of playing a part in lithium excretion are discussed. 31 references. (Journal abstract modified)

205434 Itil, M. St. Louis, MO **Computerized cerebral biopotentials in the discovery of psychotropic drugs.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):691, 1973.

A paper presented at the 8th International Congress of Electroencephalography and Clinical Neurophysiology discussed quantitative pharmacoelectroencephalography, a process involving the use of digital-computer-analyzed scalp-recorded cerebral biopotentials as well as a series of statistical procedures. The thymoleptic properties of a new compound (GB-94, N. V. Organon), which did not have pharmacological or biochemical properties of the existing antidepressive compounds was predicted. Clinical trials confirmed the prediction. Thus, GB-94 became the first psychotropic drug discovered based on an EEG model alone. The investigations indicated that computer analyses of cerebral biopotentials, particularly of relatively high frequency waves, are important parameters which reveal characteristic changes with different psychotropic drugs and with different dosages of the same compound. (Author abstract modified)

205435 Turner, M.; Morgan, J. J.; Shliapochnik, J.; Cordero Funes, J. R. Buenos Aires, Argentina, S.A. **EEG evaluation of hypnotic drugs: Mogadon v. Ro 5-4200, using the double blind method.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):691, 1973.

A paper presented at the 8th International Congress of Electroencephalography and Clinical Neurophysiology described the technique and methodology of a therapeutic clinical electroencephalogram (EEG) check and a study of sleeplessness in psychiatric affections and the comparison between the hypnotic effect of Mogadon and of a new preparation (Ro 5-4200), using the double-blind method was reported. Through the visual analysis of EEG records different REM and NREM stages (rapid sleep and slow sleep) or Phases 1, 2, 3 and 4, and rapid eye movements (REM) could be recognized and histograms or hypnograms could be elaborated. The REM phase or paradoxical sleep keeps close to the length obtained during control records. The application of hypnotic drugs resulted in an increased length of superficial sleep phases (Phases 1 and

2), with no substantial modification in either deep stage (Phases 3 and 4) or the REM phase. No statistically significant differences between the two drugs were verified, even though the need for increasing the casuistry and improving the applied methodology is stressed in order to achieve sound and reliable conclusions. (Author abstract modified)

205442 Vazquez-del-Mercado, J.; Arroyo G., H.; Calzada Z., J. Mexico City, Mexico **Electroencephalographic findings on the action of fenantyl and dehydrobenzoperidol.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):694, 1973.

A paper presented at the 8th International Congress of Electroencephalography and Clinical Neurophysiology reported a study designed to investigate the effect of fenantyl and dehydrobenzoperidol on the electrical activity of the brain, using the scalp electroencephalogram (EEG). Ten normal subjects of both sexes, aged 20-42 years, were investigated. The weights were between 55 and 70 kg. The records were obtained first in normal conditions and then during analgesia with Innovan (Fenantyl and dehydrobenzoperidol). The EEG record lasted 80 min and four groups of levels were found: 1) from 1-35 min alpha waves gradually disappeared and theta activity with normal reactivity to photic, sound and nociceptive stimulation appeared; 2) from 35-60 min, increase of theta activity from 4 to 7 c/sec, with decrease of the reactivity to photic and sound stimulation; 3) from 50-65 min alpha waves disappeared; there was predominance of theta activity and appearance of delta activity--the photic, sound and nociceptive responses markedly decreased; 4) from 65-80 min there was predominance of delta and theta activity, sometimes in bilateral paroxysms, with periodic decrease in amplitude, and no reactivity to photic, sound and nociceptive stimulation. (Author abstract)

205443 Fernandez-Guardiola, A.; Calvo, J. M.; Contreras, C. M.; Brailowsky, S.; Solis, H. Mexico City, Mexico **Heart rate and galvanic skin response variations during the REM and non-REM sleep phases in man.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):694-695, 1973.

A paper presented at the 8th International Congress of Electroencephalography and Clinical Neurophysiology reported a study which analyzed the temporal evolution of heartrate and galvanic skin response (GSR) in allnight sleep recordings in 20 healthy volunteers. In the REM phase the heartrate and the eye movements were measured every 10 sec throughout the phase duration. The relationship between the spontaneous appearance of GSR and the normal distribution of sleep phases were also studied. The results show a significant negative correlation (r) between the heartrate and the number of rapid eye movements (REMs) in REM phase. The GSR also had a tendency to increase in this phase, reaching similar levels as in the waking periods. This response reached its maximal density at the middle of the sleep time, corresponding to the second and third REM phases. These measurements were shown to be very sensitive to drug administration. Heartrate and GSR changes induced during sleep by propylhexedrine, imipramine and melatonin are described. (Author abstract modified)

205446 Kendel, K.; Cramer, H.; Wita, C. Freiburg, West Germany **Influence of melatonin on EEG and human sleep: automatic EEG analyses and polygraphic night sleep investigations.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):698-699, 1973.

A paper presented at the 8th International Congress of Electroencephalography and Clinical Neurophysiology reported a study of the acute effects of Melantonin on electroencephalogram (EEG) and sleep behavior of 15 healthy students. Automatic analysis and polygraphic recording of night sleep were performed, using a double-blind technique. Melatonin 500 mg i.v. at 21.30 was an effective sleep inducer. The mean latency of sleep onset decreased significantly from 23 min (control) to 10 min (Melatonin). The latencies of REM and deep sleep remained unchanged. No significant differences in total sleep and percentage of sleep stages and REM were observed between the control and Melatonin nights. Automatic analysis of the waking EEG could only be performed in the 10 min following the injection because later the subjects were usually asleep. Frequency spectra and amplitude histograms showed no significant variation between the Melatonin and control groups. A tendency to desynchronization, which was very pronounced in three subjects (lower amplitudes and increased higher frequencies), may be an early sign of sleep not yet detectable by visual screening. (Author abstract modified)

205460 Hirata, J.; Hosokawa, K.; Otsuki, S. Okayama, Japan **Activation of EEG by gamma-hydroxybutyrate (GHB) in organic brain disorders.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):708, 1973.

A paper presented at the 8th International of Electroencephalography and Clinical Neurophysiology reported the activation of electroencephalogram (EEG) by gamma-hydroxybutyrate (GHB) in organic brain disorders. Of 100 normal control subjects administered GHB intravenously, 85 subjects went to sleep within 15 minutes, 36 subjects showed EEGs similar to natural sleep, and 49 subjects showed a few generalized short bursts of theta waves at the stage of suppressed alpha waves. Seventy-nine patients with organic brain disorders who did not show definite EEG abnormality on routine examination were investigated under GHB activation. Fourteen with normal routine EEG showed marked abnormality under GHB activation; 43 with equivocal or minimal abnormalities in routine examination showed remarkable abnormality; and 29 showed little provoked activity. The hemisphere lesion showed the most activity, while the deep or infratentorial lesion revealed less. (Author abstract modified)

205470 Munari, C.; Frattarelli, M.; Casardi, D.; Gianasi, G. C. Paris, France **Study on amitriptyline-induced sleep in epileptic patients.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):718, 1973.

A paper presented at the 8th International of Electroencephalography and Clinical Neurophysiology reported an electroencephalographic (EEG) study of 32 epileptic patients under 0.5mg/kg of amitriptyline. The organization of amitriptyline-induced sleep varies with age. In children under 12 years of age, a complete cycle of sleep can be recorded with deep slow wave sleep (stages III and IV) and occasionally a REM phase. Such complete cycles with REM phases are exceptional in adults. In some patients clinical seizures were recorded under amitriptyline; when occurring during induced sleep, these seizures always arose during stages I or II of light sleep. Moreover, half of these patients were recorded during all-night sleep without the drug. It was thus possible to compare the patterns of amitryptiline induced sleep with the patterns of spontaneous physiological sleep in the same patients. (Author abstract modified)

205472 Roubicek, J.; Matejcek, M.; Montague, Sylvia. Basle, Switzerland **EEG changes after psychoactive drugs (spectral analytic study).** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):719, 1973.

A paper presented at the 8th International of Electroencephalography and Clinical Neurophysiology reported a spectroanalytical study of the electroencephalogram (EEG) changes after psychoactive drugs. Results of examination of reference substances (chlorpromazine, thioridazine (Melleril)) were compared with newly-developed psychoactive compounds (clozapine (Leponex), indenopyridines). Pharmacokinetic examinations done in parallel showed that the maximum concentration of Leponex in plasma corresponded in time with the peak of the EEG spectral changes in the alpha band and in the slow frequencies, as well as with behavioral changes observed over a 24-hr period after 25mg of orally-administered substance. Concentration in receptor tissue in brain, observed directly in EEG spectral variations, is more relevant for estimation of the activity of psychoactive drugs than plasma level values. (Author abstract modified)

205504 Fenelon, B.; Holland, J. T.; Johnson, C. Newcastle, Australia **Spatial distribution of the EEG of dyslexic children.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):737, 1973.

At the 8th International Congress of Electroencephalography and Clinical Neurophysiology, spatial distribution of the electroencephalogram (EEG) of dyslexic children was reported. The clinical groups were split randomly and active drug (nitrazepam) or placebo was administered to each subgroup over one of the 8 week intervals. Significant changes in S-indices of both hemispheres took place following the application or withdrawal of nitrazepam in the dyslexic subgroups but not in other groups. Improvement in scholastic achievement and general behavior was reported in more than half the dyslexic subjects during the active drug phase and EEG abnormalities decreased significantly. The more marked drug response of the dyslexic subjects supported hypotheses concerning attention-distraction factors in such children. (Author abstract modified)

205505 de Forster, E. M. C.; Suarez, M. Velasco; Nieto, D.; Castellanos, G. Mexico City, Mexico **Clonazepam (RO5-4023). Four years of clinical research.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):737, 1973.

A paper presented at the 8th International Congress of Electroencephalography and Clinical Neurophysiologydescribes a study in which 90 patients taking Clonazepam (RO5-4023) for control difficulties were selected from an epileptic clinic. Extensive records were kept on each of these patients and statistics were obtained on the most important data, e.g. general information, type and frequency of attacks previous to treatment, dosage and medicine adjustments, monthly records of the paroxysmal activity in relation to the therapy under study, and laboratory test. Special emphasis was given to electroencephalogram changes that were generally observed to coincide with the clinical data. Comments were also made on experiences obtained from a surgical case and a pregnancy, in which inadvertently an unwed mother was administered the drug during the first 16 weeks of gestation. Few habituation phenomena were manifested and no toxic effects were found, even though this product was administered in larger amounts than those recommended. (Author abstract modified)

205508 Pateisky, K.; Wessely, P. Vienna, Austria **Polygraphic examination during fast and slow intravenous injection of the same dose of diazepam.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):738-739, 1973.

At the 8th International Congress of Electroencephalography and Clinical Neurophysiology, polygraphic examination during fast and slow intravenous injection of the same dose of diazepam was reported. When diazepam was given intravenously by quick injection, the therapeutic effect in status epilepticus was less compared with the slow injection (10mg given in 10 minutes). Using diazepam in psychiatric patients for sedation, it was observed that the patients did not fall asleep when diazepam (10mg) was applied quickly, whereas with the same dose given slowly intravenously, patients fell asleep and remained so for 1 hr. Results indicate that the action of diazepam given i.v. does not depend so much on high concentration in the blood as on the time of blood passing through the brain in appropriate concentration. (Author abstract modified)

205520 Oliveros, C.; Peraita, M. R.; Reyero, F.; Calleja, J.; Vela, A.; Oliveros, A. Madrid, Spain **Comparative study of the electroneurophysiological parameters of sleep induced by several hypnotic drugs.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):753, 1973.

At the 8th International Congress of Electroencephalography and Clinical Neurophysiology, a study of the electrophysiological parameters of sleep induced by Luminal, Nembutal, a diazepoxide (Ro.4.200) and a prebarbiturate which includes in its molecule an amphetamine link (Su.42) was presented. Ro.4.200 gave a distribution of sleep very similar to that of physiological sleep. The number of spindles not modified by Ro.4.200 was large compared with the data obtained for other diazepoxides (Mogadon, Valium and Librium) which increased them. This effect was related to the presence in Ro.4.200 of a fluoride link, which did not exist in the other compounds. In computer studies of the spectral analysis produced by different drugs, the slow dominant bands disappeared after administration of Su.42, which was probably related to the amphetamine link incorporated in its molecule. (Author abstract modified)

205548 Hajnsek, F.; Faber, B. Zagreb, Yugoslavia **Further experience with Epontol in EEG activation.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):771-772, 1973.

At the 8th International Congress of Electroencephalography and Clinical Neurophysiology, the use of Epontol (Bayer), a watery solution of 3-methyl-(N,N-diethylcarbamylmethoxy)-phenyl vinegar, propyl ester, as an activating agent in electroencephalograms (EEG) was reported. This procedure was indicated first in patients with temporal lobe epilepsy or when major attacks originated in temporal or rhinencephalic structures. In the well-known Landolt's forced normalization, when the patient was psychotic, Epontol revealed the epileptic abnormalities, otherwise not detectable. Special attention was paid to the patients showing some asymmetry in the depth of sleep (according to sleep stages) over a particular region. In a group of patients sphenoidal and suboccipital derivations were applied. The possible underlying causal factors so far as the etiology was concerned were presented. (Author abstract modified)

205566 Roman, I. Bucharest, Romania **The use of Megimide in functional EEG.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):783-784, 1973.

At the 8th International Congress of Electroencephalography and Clinical Neurophysiology, a study of the use of Megimide in functional electroencephalogram (EEG) was reported. After activation a group of 19 patients (3%) was selected, with a very low convulsant threshold and frequent paroxysms of generalized spike and wave complexes (3 c/sec). In the other patients the following biolectrical alterations were recorded: 1)

isolated degraded spike and wave complexes in 14 cases; 2) unspecified irritative elements; 3) diffuse slow theta and delta dysrhythmias in 16 cases; and 4) alterations of the physiological rhythms. The tracings were not modified by Megimide in 73% of the psychiatric patients (441 cases) and 93% of the normal controls. (Author abstract modified)

205569 Tauber, J.; Wajsbort, J. Haifa, Israel **EEG changes before and after L-dopa therapy in Parkinson patients.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):784-785, 1973.

At the 8th International Congress of Electroencephalography and Clinical Neurophysiology, an analysis of the electroencephalograms (EEG) of 52 Parkinson patients treated with L-Dopa, 23 of them both before and after medication was presented. Before initiating L-Dopa, 67% of the EEGs were abnormal; these abnormal EEGs showed changes in amplitude of alpha waves in the direction flattening, as well as in their content and rhythm (alpha index). After L-Dopa therapy, abnormalities were noted in only 40% of the EEGs analysed. The off-and-on effect was noticeable in 30% of the EEGs before, and also after, treatment. Photic simulation led to an increase in wave amplitude without a driving reaction in 30% of the EEGs both before and after treatment. After L-Dopa therapy, there is an increase in frequency, amplitude and alpha wave content (alpha index), as well as reduction in beta waves and in pathological waves. (AutHor abstract modified)

205575 Vincent, O.; Deffeminis Rospide, H. A.; Scarabino, R.; Medici, M. Montevideo, Uruguay **A comparative study on the effect of intravenous diazepam and RO-5.3350 on pyramidal spasticity.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):804, 1973.

At the 8th International Congress of Electroencephalography and Clinical Neurophysiology, a comparative study on the effect of intravenous diazepam and RO-5.3350 on pyramidal spasticity was reported. Tracings were performed on several agonist and antagonist muscles, before and after i/v diazepam and RO-5.3350. Needle electrodes, temperature control and standard conditions were employed. All patients included in this study showed spontaneous activity at rest in antigravity and some agonist muscles. Saline solution was used as placebo. Both drugs decrease spasticity as shown by reduction or disappearance of spontaneous rest activity in polygraphic recording. Amounts of RO-5.3350 ranging from one third to one half, of diazepam had the same effect, which proves the first substance is more active. Intravenous injection with simultaneous electromyogram recording is a suitable procedure to compare the effect of several drugs. (Author abstract modified)

205599 Zapletalek, M.; Hubsch, T.; Zenata, L.; Strnad, D. Psychiatric Clinic, Hradec Karlove, Czechoslovakia **The effect of sydnocarb on some psychological and autonomic tests: a pilot study.** Activitas Nervosa Superior (Praha). 16(3):184-185, 1974.

At the 16th Annual Psychopharmacological Meeting, the influences of sydnocarb on some psychic functions (psychomotor speed, vigilance, performance) as well as on the autonomic nervous system were reported. After administration of sydnocarb, as compared with placebo, there is a significant increase in the tapping rate and an acceleration in the psychomotor speed in the cancellation test. In the numerical square test sydnocarb reduces time nonsignificantly. After administration of sydnocarb the mean values of orthostatic acceleration and clinostatic deceleration in the orthoclinostatic test of vagus tone and of sympathicus tone remain unchanged in comparison with placebo. It is concluded that sydnocarb accelerates psychomotor speed, increases concentration of attention and performance. However, there is no evidence of its effect on the autonomic nervous system. 3 references.

14 MECHANISM OF ACTION: BEHAVIORAL

198518 Kainuma, Hajime. Department of Neuropsychiatry, Osaka University Medical School, Dojimahamadori 3-1-2, Fukushima-ku, Osaka City, Japan 553 **Use of the Maudsley Personality Inventory in evaluating the effectiveness of a minor tranquilizer in psychosomatic diseases (the first report).** Journal of Japanese Psychosomatic Society (Tokyo). 14(3):170-174, 1974.

The Maudsley Personality Inventory (MPI) was used to evaluate the effect of diazepam on psychosomatic diseases. Fifteen patients with various psychosomatic diseases were treated with this drug for 4 weeks. After this treatment, four patients showed a marked clinical improvement, six, moderate, and five, no change. In four patients who showed marked improvement, scores of Scale E of the MPI showed a slight increase compared to the pretreatment period and a marked decrease occurred in the score in Scale N. This indicates the usefulness of the MPI in evaluating the effect of minor tranquilizers in psychosomatic diseases. 9 references. (Author abstract modified)

198592 Prange, Arthur J., Jr. no address **Thyroid axis -- drugs and behavior.** New York, Raven Press, 1974.

Current issues in drug therapy for hyperthyroid patients are reviewed, based on a colloquium of the American College of Neuropsychopharmacology. Symptoms of anxiety, irritability, fatigue and the lowering of mood displayed by hyperthyroid patients are discussed and the interactions of l-triiodothyronine with imipramine and with chlorpromazine are described. Thyrotropin-releasing hormone (TRH) and its effect on mood are mentioned. It is reported that TRH produces prompt, brief, clinical improvement in symptoms in unipolar depressed women and that TRH temporarily elevates the mood of normal women. 1 reference.

199515 Greenblatt, David J.; Shader, Richard I. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **Drug therapy: benzodiazepines (first of two parts).** New England Journal of Medicine. 291(19):1011-1015, 1974.

The pharmacological properties and clinical effects of the benzodiazepines are summarized and guidelines are offered for their rational use in clinical medicine. After a brief historical review, properties are described for chlordiazepoxide, diazepam, oxazepam, flurazepam, and clorazepate. Action is examined in terms of behavioral pharmacology, muscle relaxation, anticonvulsant effects, circulation and respiration. 20 references.

199517 Haskell, David S.; McNair, Douglas M.; Fisher, Seymour; Kahn, Richard J. Psychopharmacology Laboratory, Division of Psychiatry, Boston University Medical Center, 700 Harrison Ave., Boston, MA 02118 **A controlled outpatient trial of perphenazine-amitriptyline and chlorpromazine.** Journal of Clinical Pharmacology. 14(10):536-542, 1974.

A 4-week comparison of the combination perphenazine-amitriptyline and chlorpromazine in the treatment of anxious, nonpsychotic outpatients was conducted which showed minimal significant drug differences. Although small but consistent trends favored the combination agent in the sample as a

whole, it was significantly less beneficial on a few measures in patients with coexisting depression. A high incidence of drowsiness was observed with both medications. The high dropout rate resulted in small samples for comparing the medications. 9 references. (Author abstract)

199518 Stephens, Joseph H.; Shaffer, John W.; Brown, Clinton C. Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **A controlled comparison of the effects of diphenylhydantoin and placebo on mood and psychomotor functioning in normal volunteers.** Journal of Clinical Pharmacology. 14(10):543-551, 1974.

In a double-blind investigation, the effects of diphenylhydantoin (DPH) and placebo on mood and psychomotor functioning in 107 normal volunteers were compared. DPH was given in dosages of 100mg three times daily for 2-week periods, and subjects were evaluated both before and after medication on 29 measures of mood, symptomatology, and affect and nine measures of psychomotor coordination and intellectual functioning. The experimental design employed permitted an empirical test of the relative sensitivity of two widely-used statistical analyses: the two-period changeover and the analysis of covariance. Separate analyses by sex were also performed. With one exception, results based on the covariance analyses did not attain statistical significance; the two-period changeover analyses yielded significant treatment mean differences on 10 of the 29 dependent variables measuring mood, symptomatology and affect but on only one of the nine dependent variables measuring psychomotor coordination and intellectual functioning. For the male group separately, treatment differences were essentially nonsignificant. In females, DPH appeared to produce mildly dysphoric effects similar to those produced by certain minor tranquilizers in normal subjects. 23 references. (Author abstract modified)

199609 Stix, Allen H. Scarsdale, NY **Chlordiazepoxide (Librium): the effects of a minor tranquilizer on strategic choice behavior in the Prisoner's Dilemma.** Journal of Conflict Resolution. 18(3):373-394, 1974.

The effects of two dosages of a widely-used tranquilizer, chlordiazepoxide (marketed as Librium), on strategic choice behavior in the Prisoner's Dilemma, are reported relative to a placebo control group and a no-capsule control group. Present results are compared with those from an earlier study of drug effects on gaming by Hurst et al. in an attempt to begin developing a broader idea as to the effects of different varieties of psychopharmacological drugs on strategic interchanges. Sociopharmacology is discussed as a social scientific specialization centered upon studying the effects of mind-affecting drugs on the person as a social actor and the courses followed by social processes. 18 references. (Author abstract)

199663 Spohn, Herbert E.; Lacoursiere, Roy B.; Williams, Roger O. Menninger Foundation, Box 829, Topeka, KS 66601 **The effect of chlorpromazine on visual information processing in normal subjects.** Journal of Nervous and Mental Disease. 159(3):198-204, 1974.

The hypothesis that chlorpromazine (CPZ) has the effect in visual information processing of protecting the short-term memory (STM) visual trace by serving to filter or habituate stimuli following an initial stimulus was tested in 40 normal college students. The method involved the tachistoscopic presentation of paired, successive 3 x 2 consonant arrays, separated by a 200 msec interval, with instructions to report either the first or the second array, in a double-blind repeated measurement design in which subjects served as their own placebo controls and a single dose of 50mg of CPZ was administered. The results do not support the hypothesis, but suggest that when ipsimodal, isomorphic distraction follows an initial relevant stimulus, CPZ tends to reduce STM span. The results do afford partial support for the hypothesis that CPZ has the effect of delaying the processing (coding) of visual information. A CPZ mechanism of action on response criteria in deciding the relevance of stimuli is advanced and related to clinical effects of CPZ in acute schizophrenics. 13 references. (Author abstract)

199896 Morland, J.; Setekleiv, J.; Haffner, J. F. W.; Stromsaether, C. E.; Danielsen, A.; Wethe, G. Holst. Institute of Pharmacology, University of Oslo, Oslo, Norway **Combined effects of diazepam and ethanol on mental and psychomotor functions.** Acta Pharmacologica et Toxicologica (Kobenhavn). 34(1):5-15, 1974.

The performances of eight healthy young males were tested 1-3 hrs after oral administration of placebo, 10mg diazepam, ethanol or the same amount of ethanol combined with 10mg diazepam. Both ethanol and diazepam reduced concentration, efficiency, and attention (Osgood Test). Combined administration augmented this subjective impression, and also reduced motivation. Ethanol significantly reduced the score in the minor tracing test, and diazepam significantly reduced the score in the letter cancellation, flicker fusion frequency, and mirror tracing tests, and in the clinical examination. Combined administration of ethanol and diazepam increased the detrimental effects on the tests mentioned above, and also increased the effect on time evaluation ability and complex coordination and sorting tests. Generally diazepam slowed the subjects, ethanol speeded them up, but increased their errors, combined administration both slowed them up, and increased their errors. 6 references. (Author abstract modified)

199989 Hansen, Villy; Ravn, Jorgen; Rud, Christian. Department K, Mental Hospital, Middelfart, Denmark **Long-term treatment of psychiatric patients with clopenthixol: analysis of laboratory tests with a view to long-term therapy.** Acta Psychiatrica Scandinavica (Kobenhavn). 50(3):309-317, 1974.

In a study of the effects of long-term therapy with clopenthixol in terms of measurable laboratory parameters, 57 female patients who had been treated with clopenthixol alone from 3 to 9 years were examined. Twenty-six patients had psychiatric diseases only and 31 had concomitant somatic diseases. Several parametric and nonparametric statistical methods (especially Spearman's Rho) were used to study the relationships between the measured values, in particular variations within the normal range between the two groups. Age, dose and duration of treatment were variables along with laboratory tests. There were no indications that long-term treatment with clopenthixol exerts a nephrotoxic, hepatotoxic, or hematotoxic 14 MECHANISM OF ACTION: BEHAVIORAL; effect. Changes did seem to occur in certain parameters, predominantly within the range of normal, especially as concerns thymol turbidity values and total leucocyte count. 7 references. (Author abstract modified)

200007 Caldwell, John; Sever, Peter S. Department of Biochemistry, St. Mary's Hospital Medical School, London **The biochemical pharmacology of abused drugs. II. Alcohol and barbiturates.** Clinical Pharmacology and Therapeutics. 16(5):737-749, 1974.

Problems associated with the excessive consumption of alcohol and barbiturates are discussed. Although a wide range of

sedatives are misused, the problem is seen principally with the barbiturates. While many aspects of the biochemical pharmacology of alcohol and of the barbiturates are widely dissimilar, there is a considerable cross-tolerance between them and they are alike in that rapid development of tolerance can occur as the result of a single exposure to either of them. 66 references. (Author abstract modified)

200048 Huntley, M. Stephen, Jr. DOT Transportation Systems Center, Code: TIF, Kendall Square, Cambridge, MA 02142 **Effects of alcohol, uncertainty and novelty upon response selection.** Psychopharmacologia (Berlin). 39(3):259-266, 1974.

The effects of alcohol, uncertainty and novelty upon response selection were studied. Following consumption of an alcohol or placebo beverage, one group of twelve subjects made familiar and a second group of twelve made novel responses to tachistoscopically-presented letters from stimulus groups comprised of two, four or eight letters. It was found that blood alcohol concentrations approximating 80 mg/100ml have little effect on letter identification times when stimulus-response associations are highly familiar. When associations are novel, identification times are increased by alcohol and the magnitude of the increase is logarithmic (log2) with the number of equally likely stimulus-response pairs. When obtained, alcohol effects retard selection of the identification response rather than influencing stimulus recognition per se. 14 references. (Author abstract)

200057 Liljequist, R.; Linnoila, M.; Mattila, M. J. Department of Psychology, University of Helsinki, Helsinki, Finland **Effect of two weeks' treatment with chlorimipramine and nortriptyline, alone or in combination with alcohol, on learning and memory.** Psychopharmacologia (Berlin). 39(2):181-186, 1974.

In a study of learning and memory, 20 male students were treated double-blind crossover with nortriptyline, chlorimipramine, or placebo for 2 weeks. Alcohol alone significantly increased the numbers of mistakes in paired-associate learning test. Nortriptyline alone slightly increased the numbers of mistakes in paired-associate learning test and impaired backward recall of digits. Chlorimipramine alone had no measurable effect on learning or memory. Nortriptyline enhances the deleterious effect of alcohol on the ability to learn new material, whereas chlorimipramine antagonized alcohol in this respect. Both antidepressants significantly shifted the dose response graph for the tyramine effect on systolic blood pressure to the right. 20 references. (Author abstract modified)

201909 Aleksandrovskiy, Yu. A.; But, P. G.; Kaplunskiy, G. D.; Poltorakov, A. P.; Chibrikin, V. M. Moskovskii nauchno-issledovatal0skii institut psikhiatrii, Moscow /**Comparative characteristics of the clinical action of tranquilizers.**/ Sravnitel0naya kharakteristika klinicheskogo deystviya trankvilizatorov. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 74(9):1389-1397, 1974.

The actions of various tranquilizers are compared. Meprobamate, trioxazine, diazepam, chordiazepoxide, oxazepam, nitrazepam, medazepam, lorazepam, and tacitine were administered to 383 patients with borderline conditions. Multivectoral graphic analysis of the tranquilizing effects was used to rank the tranquilizers' effects. Knowledge of their characteristics and general and selected actions may serve as a basis for rational choice of tranquilizers in different areas of clinical practice. 4 references. (Journal abstract modified)

201916 Zakharova, N. N. Laboratoriya patofiziologii vysshey nervnoy deyatel0nosti, Moscow /**The effect of seduxen on the perceptive and some other functions of the central nervous system under emotional stress in man.**/ Vliyaniye seduksena na nekotoryye funktsii tsentral0noy nervnoy sistemy v usloviyakh emotsional0nogo stressa u cheloveka. Farmakologiya i Toksikologiya (Moskva). 37(4):396-398, 1974.

The effect of seduxen on emotional stress and on perception of sensory signals, EEG, and some autonomic functions was studied in men. Used in therapeutic doses, seduxen is shown to have marked influence on the emotions without significantly affecting other physiological functions. It is concluded that seduxen is relatively selective in its action on the integration of emotional behavior. 8 references. (Journal abstract modified)

202285 Sakamoto, Fujio; Yoshimura, Masahiro. School of Medicine, Kogoshima University, Japan **Treatment and countermeasures for patients with insomnia in the department of internal medicine -- special emphasis on the clinical application of flurazepam.** Medical Consultation and New Remedies (Tokyo). 10(4):93-107, 1973.

The hypnotic effects of flurazepam were studied in an experiment in which 20 patients with internal disorders and insomnia were orally treated with flurazepam (10 or 20mg) once a day for 2 weeks. Except for three patients, all the patients treated with 10mg of the drug fell asleep within 45 minutes. Most of the patients experienced a significant decrease in interruption of sleep and had less difficulty returning to sleep; however, those treated with 20mg a day had less trouble in returning to sleep. Those treated with 10mg a day had dreams on a total of 88 days and those treated with 20mg, 62 days. Most of the patients slept more than 7 hours a day. A few minor side-effects, such as sense of fatigue, dizziness and drowsiness in daytime, were observed. 8 references.

202784 Dittrich, A.; Woggon, B. Aus der Psychiatrischen Universitatsklinik Zurich, Burgholzli, Lenggstrasse 31, CH-8008 Zurich /**Subjective changes in volunteers without prior experience of cannabis induced by (-)delta9-trans-tetrahydrocannabinol.**/ Subjektive Veranderungen unter (-)delta9-trans-Tetrahydrocannabinol bei cannabisnaiven Probanden. International Pharmopsychiatry (Basel). 9(3):138-151, 1974.

Students with no prior experience of cannabis received either delta9-tetrahydrocannabinol (THC) or placebo, orally, in a double-blind study, in order to assess the high dosage effects of THC. THC caused profound depersonalization and derealization syndromes. Anxious-depressive and euphoric-stimulated states occasionally appeared during one intoxication, at approximately the same time, and/or at different times. Some subjects, with their eyes closed, had optical hallucinations which could be influenced by suggestion. The tests used, as well as the behavior observation of the subjects, showed a great interindividual and intraindividual variability of the intensity of THC effects. Two hours after application of the drug, the following subjective side-effects were observed: weariness and feebleness, heaviness of the legs, dizziness and hypersensitivity against cold. While no difference between THC and placebo was found in the self-assessed changes of the ability to concentrate, the results of the test show a significant decrease of performance under THC. 23 references. (Author abstract)

202886 Carman, John S.; Post, Robert M.; Teplitz, Terry A.; Goodwin, Frederick K. Adult Psychiatry Branch, NIMH, 9000 Rockville Pike, Bethesda, MD 20014 **Divalent cations in predicting antidepressant response to lithium.** Lancet (London). 2(7894):1454, 1974.

The relation between magnesium and calcium and subsequent antidepressant response to lithium is examined in depressed hospital patients. Both the pretreatment plasma magnesium and calcium levels and changes in these ions during the first 5 days of lithium therapy were examined. The pretreatment calcium/magnesium ratio was significantly related to subsequent antidepressant response to lithium. The clinical value of the findings must be confirmed in larger studies, but the low frequency of false positives and false negatives suggests that these changes should be clinically useful. It is not yet known whether acute antidepressant response will be predictive of ultimate prophylactic response. The findings also provide further evidence consistent with the suggested importance of magnesium and/or calcium in the mechanism of action of lithium and ultimately in the pathophysiology of affective illness. 18 references.

202887 Ehrensing, Rudolph H. Department of Psychiatry, Ochsner Clinic, New Orleans, LA 70121 **Lithium and M.R.I.H. in tardive dyskinesia.** Lancet (London). 2(7894):1459-1460, 1974.

A patient with tardive dyskinesia is described who has experienced prolonged response to lithium carbonate, and some hypotheses regarding the possible role of lithium and melanocyte-stimulating hormone release inhibiting hormone-I are suggested. The gradual improvement of this patient's tardive dyskinesia over the initial weeks of treatment is consistent with results of animal studies and the general improvement seen in mania when lithium is given.

203599 Giovannetti, A.; Trombetta, N. Via Portico D'Ottavia 9, Rome, Italy **Pretreatment of problem youths with clozapine in preparation for group psychotherapy.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 7(5):230-236, 1974.

The extent to which the tranquilizer Clozapine facilitated psychotherapy in an open pilot study of 35 patients and a blind study on 40 children is reported. Results show that the effects of the drug outlast the treatment. Clozapine helped to eliminate such symptoms as pavor nocturnus, dysthymia, irritability, aggressiveness and anxiety. Patients handled frustrations better and they became more attentive and were able to concentrate better. It is concluded that pretreatment with the drug facilitated psychotherapy. 12 references.

203601 Konig, L.; Rossner, M. Fachambulanz der Medizinischen Akademie "Carl Gustav Carus" Dresden, 8019 Dresden, Fetscherstr. 74, Germany /**Changes in the psychodynamics of manic-depressives through long-term administration of lithium salts.**/ Veranderungen in der Psychodynamik manisch-depressiver Erkrankungen durch langfristige Anwendung von Lithiumsalzen. Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 7(5):248-253, 1974.

The effects of long-term treatment of manic-depressive patients with lithium salts is discussed. Under long-term treatment, reappearing manic-depressive phases show a shorter course or less marked symptoms. Patient behavior and ways in which they cope with their lives show marked improvement. A mixture of undisturbed personality features, secondary reaction and symptom formation may result in new problems for the patient in his correlation to his environment. 18 references. (Author abstract modified)

203603 Itil, Turan M.; Saletu, B.; Marasa, J. 150 White Plains Road, Tarrytown, NY 10591 **Determination of drug-induced changes in sleep quality based on digital computer "sleep prints".** Pharmakopsychiatrie Neuro-Psychopharmacologie (Stuttgart). 7(5):265-280, 1974.

The effects of flurazepam, methaqualone and triazolam, a new triazolobenzodiazepine, on the subjectively-evaluated quality of sleep, as well as on objective sleep parameters were investigated in normal healthy volunteers and compared to placebo. It was found that methaqualone, flurazepam and triazolam produced computer EEG profiles similar to those seen after minor tranquilizers, with the profile of flurazepam being the least characteristic. Correlation statistics demonstrated that a drug can be regarded as an ideal hypnotic if it decreases awakenings and stage 1 sleep, does not attenuate stage 4 sleep significantly, decreases the average frequency in the EEG, increases the length of REM periods and decreases REM bursts. The criteria were best met by flurazepam and triazolam. Side-effects increased with increased dosages. Sleep stage lengths are not dose-related nor helpful in discriminating the active drugs from placebo. 40 references. (Author abstract modified)

203704 Broeker, Harald; Sack, Gerhard; Muller, Detlef; Muller, Jutta. Neurologish-Psychiatri sc he Klinik der Medizinischen Akademie "Carl Gustav Carus", DDR-8019 Dresden, Festcherstrasse 74, Germany /**Sleep-EEG tests of nonspecific cases of paroxysm and episodic behavioral disturbances: a preliminary report.**/ Schlaf-EEG-Untersuchungen bei unklaren Anfallszustanden und episodischen Verhaltensstorungen: ein vorlaufiger Bericht. Psychiatrie, Neurologie und medizinische Psychologie (Leipzig). 25(11):656-660, 1973.

The particular practical importance of further clarification in patients suffering from nonspecific cases of paroxysm and episodic irritation and depressions is discussed. Patients who in initial EEG tests (rest, hyperventilation and photostimulation) did not indicate a defined top potential were given, after a night of sleep deprivation, a dose of at least two Dormutil tablets and sleep deviation with subsequent hyperventilation was conducted. Out of 665 tests, 34 cases during sleep and a further 12 cases during subsequent hyperventilation showed safe proof of top potential, i.e. 6.9%. 14 references. (Journal abstract modified)

203840 Bente, D.; Feder, J.; Helmchen, H.; Hippius, H.; Mauruschat, W. Abteilung fur Psychophysiologie der Freien Universitat Berlin, 1 Berlin 19, Nussbaumallee 34, Germany /**Multidimensional psychopharmacotherapeutic trials with the neuroleptic Perazine. 2. Communication: psychopathological course profile and somatic characteristics (studies with the AMP system).**/ Multidimensionale pharmakopsychiatrische Untersuchungen mit dem Neuroleptikum Perazin. 2. Mitteilung: Verlaufsprofile psychopathologischer und somatischer Merkmale (Untersuchungen mit dem AMP-System). Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 7(1):8-17, 1974.

A 30-day Perazine treatment for 49 patients is analyzed and reported. Target symptoms of Perazine are delusional phenomena, tension, anxious affect, failings in formal thinking processes and hallucinations. All of the symptoms were reduced. No side-effects such as weariness, mouth dryness and vertigo were noted. The differentiated registration of psychopathological items with the aid of the well-defined improvement and provocation quotients (BQ and PQ) during the course of treatment is a precondition for diagnostic correlations which build upon course profiles of single parameters. 11 references. (Author abstract modified)

203847 Carpenter, Robert L.; Sells, Clifford J. Child Development and Mental Retardation Center, University of Washing-

ton (WJ-10), Seattle, WA 98195 **Measuring effects of psychoactive medication in a child with a learning disability.** Journal of Learning Disabilities. 7(9):545-550, 1974.

The application of several customary measurement techniques used with a child receiving psychoactive medication is described. The three types of behavior measured were short-term memory, response latency, and attention. For the child described, the medication used was shown to have no clinically significant effect on her performance on these measures. The report demonstrates that some basic principles employed in well-designed studies of drug effectiveness are easily adaptable to the clinical situation; namely, a double-blind design, placebo control, multiple dosage levels, and objective measurement of behavior. 10 references.

203881 Remschmidt, Helmut; Remschmidt, Ursula. Klinik fur Kinder- und Jugendpsychiatrie, Philipps Universitat, 355 Marburg/Lahn, Hans-Sachs-Strasse 4-6, Germany /**Signs, course and prognosis of tics in children and juveniles.**/ Symptomatologie, Verlauf und Prognose von Ticerkrankungen im Kindes- und Jugendalter. Klinische Padiatrie (Stuttgart). 186(3):185-199, 1974.

Signs, course and prognosis of tics in children and juveniles during a 3-year study are reported. Parent answers to a standard inquiry as to the course of the illness are included. Twenty-four patients had been treated with drugs; 29 were treated without drugs. Although early successes with butyrophenone preparations, particularly with haloperidol, were impressive, there was no difference between later results in those treated and untreated. 60 references. (Journal abstract modified)

204405 Boucsein, W. Psychologisches Institut der Universitat Dusseldorf, 4 Dusseldorf, Universitatsstr. 1, Germany /**The action of chlordiazepoxide on conditions of anxiety in a psychophysiological experiment.**/ Die Wirkung von Chlordiazepoxyd unter Angstbedingungen im psychophysiologischen Experiment. Arzneimittel-Forschung (Aulendorf). 24(8):1112-1114, 1974.

The anxiety-reducing property of chlordiazepoxide was investigated under two anxiety-evoking conditions, and compared with a control condition. Subjects were told to expect an electric shock twice as heavy under one condition and five times as heavy under the other condition in relation to a shock they had received before. During the anticipation phase, all subjects had to observe a clock and continuously scale their emotional excitement; heartrate, galvanic skin resistance and breathing rate were also registered continuously. The results show a tendency for chlordiazepoxide to reduce emotional excitement more in the group that expected the heavier shock than in the other ones, with some paradoxical effects under control conditions. Interactions between anxiety conditions and medication were observed only at the beginning of the anticipation phase. 8 references. (Journal abstract modified)

204412 Fleischhauer, J.; van Riezen, H. Psychiatrische Universitatsklinik, Basel, Switzerland /**Studies on clinical and pharmacological spectra of the tetracyclic compound mianserin.**/ Untersuchungen zum klinischen und pharmakologischen Wirkungsbild der tetrazyklischen Substanz Mianserin. Arzneimittel-Forschung (Aulendorf). 24(8):1129-1131, 1974.

Features of mianserin, GB-94, a tetracyclic clinically-effective antidepressant with a pharmacological spectrum unlike that of the known tricyclic antidepressants, are described. In its clinical spectrum, mianserin has mood-elevating, anxiolytic, and slight sedative properties; no side-effects were observed. The onset of the drug's efficiency is within a few days, at an optimum dosage of 10mg to 40mg. 4 references. (Journal abstract modified)

205135 Holt-Hansen, Kristian. Psychological Laboratory, University of Copenhagen, 3 Dyrkob, DK-1166 Copenhagen K, Denmark **Duration of experienced lengthening and shortening of straight lines.** Perceptual and Motor Skills. 39(2):987-996, 1974.

The duration of experienced lengthening and shortening of straight lines was studied. Results reveal that barbiturates cause significant increases in duration of lengthening-shortening. It is suggested that this is consistent with the notion that the source of the experienced lengthening-shortening is to be found in cortical brain processes. An electronic explanation of the experienced movement as a working hypothesis is offered. 2 references. (Author abstract modified)

205223 Mitchell, Valerie E.; Ross, Sherman; Hurst, Paul M. Howard University, Washington, DC **Drugs and placebos: effects of caffeine on cognitive performance.** Psychological Reports. 35(2):875-883, 1974.

The effects of caffeine alkaloid on cognitive performance were investigated. Previous experiments indicate that caffeine reduces drowsiness and increases alertness. It was hypothesized that 300mg of caffeine would enhance performance on the Paced Sequential Memory Task. Subjects, 60 volunteer college students taking undergraduate psychology courses, were randomly assigned to four treatment groups: 1) drug; 2) drug disguised; 3) placebo; and 4) no drug. Subjects were instructed on the nature of the task, then tested individually. The original data analysis showed no statistically reliable effects, despite a considerable spread of treatment means. Due to extremely high within-groups variance, the data were reanalyzed with outliers removed according to Grubbs' (1950) criterion. A significant interaction was found between presence of drug and presence of pill, suggestive of an active placebo effect in the direction of performance enhancement. It is noteworthy that such an effect would be misinterpreted in the conventional drug versus placebo model. 13 references. (Author abstract modified)

205263 Cole, Sherwood O. Psychology Dept., Rutgers University, Camden, NJ 08102 **Hyperkinetic children: the use of stimulant drugs evaluated.** American Journal of Orthopsychiatry. 45(1):28-37, 1975.

The use of stimulant drugs in treating hyperkinetic children is briefly reviewed. It is felt that, while drugs appear to be effective in normalizing behavior, too little attention has been paid to potential side-effects. It is concluded that there is a need for a broader program of clinical evaluation, assessing drug effects not only on behavior, but on appetite and the cardiovascular system, and taking into account the sociological impact of drug use by children. 35 references. (Author abstract modified)

205264 Schleifer, Michael; Weiss, Gabrielle; Cohen, Nancy; Elman, Meryl; Cvejic, Helen; Kruger, Elena. Dept. of Psychology, Montreal Children's Hospital, 2300 Tupper Street, Montreal, Quebec, Canada **Hyperactivity in preschoolers and the effect of methylphenidate.** American Journal of Orthopsychiatry. 45(1):38-50, 1975.

The effect of methylphenidate on hyperactivity in preschoolers was investigated. Observations of nursery behavior and tests of cognitive style and motor impulsivity

were carried out with 28 hyperactive preschool children of normal intelligence and 26 matched control children. The hyperactive group was also observed and tested on methylphenidate and placebo. Methylphenidate was found to reduce hyperactivity at home, but it did not improve nursery behavior or psychological functioning. Unwanted side-effects made the drug less useful at this age than in older hyperactive children. 19 references. (Author abstract modified)

15 TOXICOLOGY AND SIDE EFFECTS

200492 Blumberg, Michael Z.; Young, Stuart. National Jewish Hospital, 3800 East Colfax Avenue, Denver, CO 80206 **Diazepam-associated asthma.** Pediatrics. 54(6):811-812, 1974.

An asthmatic reaction apparently resulting from immediate hypersensitivity to diazepam (Valium) is reported. It is suggested that this case is of interest because attempts to document immediate hypersensitivity reactions to drugs are uncommon, penicillin being the only well known exception. 12 references.

200572 Schwartz, R. Burkhardt. Neurologische Universitatsklinik, Hamburg-Eppendorf, D-2000 Hamburg 20, Martinstr. 52, Germany /**EEG variations under antabuse (disulfiram) and antabuse plus alcohol exposition: a study of pathogenesis from antabuse therapy complications.**/ EEG-Veranderungen unter Antabus (Disulfiram) und Antabus-Alkohol-Exposition: Ein Beitrag zur Pathogenese von Antabus-Behandlungs-Komplikationen. Nervenarzt, (Berlin). 45(8):436-440, 1974.

Systematic electroencephalographic examinations were conducted in 32 patients with varying degrees of alcoholism. In 25% of the subjects, antabuse or antabuse plus alcohol produced a rise in cerebral activity and a decline in cerebral activity in another 25%. A primary cerebral excitement effect by antabuse is contraindicated. Courser EEG changes, as described in literature elsewhere, could not be observed. The pathogenesis of cerebral treatment complications is discussed with advice against antabuse administration to epileptic patients. Impressive blood circulation reactions while under alcohol plus antabuse administration were not noted, but still might play a role in the development of cerebral complications. 27 references.

200573 Bauer, G.; Nowak, H.; Polaczek, R. Psychiatrische und Neurologische Univ.-Klinik, A-6020 Innsbruck, Austria /**Polyneuropathy as a result of diphenylhydantoin overdose.**/ Polyneuropathie durch Diphenyl-Hydantoin-Uberdosierung. Nervenarzt (Berlin). 45(8):441-444, 1974.

Polyneuropathies occurring in two temporal lobe epileptic patients after treatment with the anticonvulsive drug diphenylhydantoin are discussed. These complications do not contraindicate a skillful use of the diphenylhydantoin. The dosage does deserve careful attention, especially when in combination with other anticonvulsive drugs. An alternate etiology for these polyneuropathies could not be found. A reduced dosage of diphenylhydantoin over a 6-month period considerably reduced paresis in one patient, but not in the other. 39 references.

200952 Waldmann, K. -D.; Greger, J.; Kluge, H.; Groschel, W.; Zahlten, W.; Hartmann, W. Universitats-Nervenklinik, Philosophenweg 3, DDR-69 Jena, Germany /**Study of lithium intoxication under therapeutic lithium serum concentration.**/ Beitrag zur Lithiumintoxikation bei therapeutischer Lithium-Serum-Konzentration. Psychiatria Clinica (Basel). 7(1):56-62, 1974.

Toxic manifestations are reported, occurring during prophylactic lithium treatment, of a woman with periodic depressions. They appeared as neurological and gastrointestinal symptoms as well as an organic psychosyndrome while the serum lithium level was within therapeutic levels. The connection of the earlier mentioned symptoms and the lithium therapy could be established; the organic psychosyndrome appeared also to be due to the lithium. Particular aspects of the relations between lithium dosage and lithium serum levels, as well as changes in the potassium serum levels for the entire time of the treatment are described and discussed. 12 references. (Journal abstract)

201239 Noble, Peter. Maudsley Hospital, London, SE5 8AZ, England **Depressive illness and hyperparathyroidism.** Proceedings of the Royal Society of Medicine (London). 67(10):1066-1067, 1974.

At the January 11, 1974 meeting of the Royal Society of Medicine, two episodes of depressive illness in a 53-year-old woman suffering from hyperparathyroidism were reported. The first illness occurred during the course of reserpine treatment, and the second within 1 month of stopping trimipramine. The second illness failed to respond to either tricyclic medication or electroconvulsant treatment, and the patient was hypercalcemic. She made a rapid response to trimipramine after parathyroidectomy. It is noted that, in the mangement of an organically determine psychosis, attention must be given both to the treatment of the undelying physical cause and the presenting psychiatric syndrome. 3 references.

201260 Toru, Michio. Department of Neuropsychiatry, Tokyo Medical and Dental University School of Medicine, Japan **Side-effects of psychotropic drugs -- an analysis of data obtained from double-blind comparative studies in Japan.** Clinical Psychiatry (Tokyo). 16(7/8):659-664, 1974.

The literature on side-effects of psychotropic drugs is reviewed. Types and frequency of occurrence of side-effects induced by phenothiazine derivatives, tricyclic antidepressants and benzodiazepine derivatives are considered. 26 references.

201287 Cohen, Wendy J.; Cohen, Norman H. Dept. of Neurology, New York Medical College-Metropolitan Hospital Center, New York, NY **Lithium carbonate, haloperidol, and irreversible brain damage.** Journal of the American Medical Association. 230(9):1283-1287, 1974.

Effects of a combined regimen of lithium carbonate and high doses of haloperidol are reported for four acutely agitated patients with diagnoses of mania. At least 50 other patients had been similarly treated without reported adverse effects, but in these four, severe encephalopathic syndromes developed. Symptoms consisted of lethargy, fever, tremulousness, confusion, and extrapyramidal and cerebellar dysfunction, accompanied by leukocytosis and elevated levels of serum enzymes, blood urea nitrogen, and fasting blood glucose. Two patients suffered widespread, devastating, irreversible brain damage; two others were left with persistent dyskinesias. Causal factors have not been identified. 30 references. (Author abstract modified)

201911 Gol0dovskaya, I. L. Institut psikhiatrii, Academy of Medical Sciences, Moscow /**Possibilities and limitations of psychotropic therapy in patients with glaucoma.**/ O vozmozhnostyakh i ogranicheniyakh terapii psikhotropnymi sredstvami lits, stradayushchikh glaukomoy. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 74(9):1402-1405, 1974

The effects of psychotropic drugs on glaucoma were studied to determine which ones could be used safely. Subjects were 57 patients suffering from different mental disorders and glaucoma. The two types of glaucoma (open angled and closed angled) reacted differently to anticholinergic drugs (mainly tricyclic antidepressants). Danger of decompensation of the process existed only in closed angled glaucoma; even long-term use of the drugs was safe in open angled glaucoma. The existing view that glaucoma is an absolute contraindication to the use of tricyclic antidepressants and other psychotropic drugs is challenged. 19 references. (Journal abstract modified)

202310 Learoyd, Brian M. North Ryde Psychiatric Centre, North Ryde, N. S. W. 2113 **Psychotropic drugs -- are they justified?** Medical Journal of Australia (Sydney). 1(13):474-479, 1974.

A brief review of the evidence supporting the efficacy of psychotropic drugs is presented. Drugs are considered from the following viewpoints: mechanism of action; efficacy; disadvantages of cost, addiction potential, social withdrawal, drug interaction, self-poisoning potential and specific toxic reactions. The high frequency of psychogeriatric admissions directly attributable to psychotropic drug intoxication was noted. Emphasis was placed on the drugs' disinhibiting effects which, while common, were not generally recognized. 54 references. (Author abstract modified)

202445 Lambert, P.-A. Hopital Psychiatrique, 73-Bassens, Chambery, France /**The extrapyramidal syndrome induced by neuroleptics.**/ Le syndrome extra-pyramidal induit par les neuroleptiques. Encephale (Paris). 62(1):78-105, 1973.

The extrapyramidal syndrome, induced by neuroleptics, is examined, focusing on the different disturbances and their treatment. The drugs are classified according to whether their effects are sedative or incisive. The evolution of temporal disturbances is described. Parkinsonian-like disturbances caused by the neuroleptics assume two forms: a mild form with akinetic predominance, and an akineto-hypertonic form. Other disturbances include the hyperkineto-hypertonic syndrome, dyskinesias or tardive hyperkinesias, and chronic irreversible dyskinesias. Paroxysmal excito-motor attacks are very sensitive to neuroleptics. The hypertonic syndrome is generally very sensitive to antiparkinsonian drugs if the dosage is high enough. Tremor is less regularly sensitive than hypertonia. Chronic hyperkinetic or dyskinetic manifestations are not altered by the antiparkinsonian drugs; akinesia is not always reduced by the use of antiparkinsonian drugs. 22 references.

202764 Kelly, John T.; Zimmermann, Robert L.; Abuzzahab, Faruk S.; Schiele, Burtrum C. University of Minnesota Hospitals, Department of Psychiatry, Box 381 Mayo, Minneapolis, MN 55455 **A double-blind study of amantadine hydrochloride versus benztropine mesylate in drug-induced Parkinsonism.** Pharmacology (Basel). 12(2):65-73, 1974.

A double-blind crossover comparison of the relative efficacies of amantadine hydrochloride and benztropine mesylate was performed on a sample of patients showing parkinson-like side-effects secondary to the administration of antipsychotic drugs. Clinical evaluations of parkinson-like side-effects showed no difference in efficacy between the two drugs. While both clinical impressions and statistical analyses show benztropine mesylate to be more effective, both drugs show efficacy in reducing drug-induced parkinson-like side-effects. 16 references. (Author abstract)

202919 Burks, Jack S.; Walker, Jonathan E.; Rumack, Barry H.; Ott, John E. Dept. of Neurology, Veterans Administration Hospital, Denver, CO **Tricyclic antidepressant poisoning: reversal of coma, choreoathetosis, and myoclonus by physostigmine.** Journal of the American Medical Association. 230(10):1405-1407, 1974.

Two patients with coma, choreoathetoid movements, and myoclonus due to tricyclic antidepressant poisoning, were treated with physostigmine salicylate, a centrally-active anticholinergic agent, which reversed the neurologic abnormalities. Physostigmine is recommended for treating tricyclic antidepressant poisoning as well as for treating classical anticholinergic intoxication. It is relatively safe and can be used as a diagnostic test for suspected poisoning from these agents. The cases also support the cholinergic deficiency/dopaminergic excess hypothesis of chorea. 20 references. (Author abstract modified)

202921 Adler, Sheldon. 3459 Fifth Ave., Pittsburgh, PA 15213 **Methyldopa-induced decrease in mental activity.** Journal of the American Medical Association. 230(10):1428-1429, 1974.

Disturbances in mental acuity were reported in five professional people receiving methyldopa. The patients had not received an excessive dosage of methyldopa, as judged by the response to therapy and the conventional amount given. When treatment with this drug was discontinued, the mental symptoms disappeared within 96 hours. The cases emphasize the importance of questioning patients taking methyldopa about difficulties in mentation. 12 references. (Author abstract modified)

202922 Snyder, Bruce D.; Blonde, Lawrence; McWhirter, William R. Dept. of Neurology, Univ. of Minnesota School of Medicine, St. Paul-Ramsey Hospital, 640 Jackson St., St. Paul, MN 55101 **Reversal of amitriptyline intoxication by physostigmine.** Journal of the American Medical Association. 230(10):1433-1434, 1974.

Reversal of coma due to amitriptyline hydrochloride overdose by the administration of physostigmine salicylate is discussed. Physostigmine is the only commonly-used specific cholinesterase inhibitor that readily penetrates the blood-brain barrier. Physostigmine rapidly restored alertness and reversed tachycardia in several patients with amitriptyline intoxication. Two cases are described which reinforce the concept that physostigmine is useful to treat poisoning from tricyclic antidepressants. Anticholinergic agents were used to correct or prevent side-effects from the physostigmine. 4 references.

203494 Barbeau, A. no address /**Contribution of treatment by levo-dopa to the neuropharmacology of akinesia.**/ Contribution du traitement par la Levo-DOPA a la neuropharmacologie de l'akinesie. Medecine et Hygiene (Geneve). 30:1844-1845, 1972.

Fifty sufferers from akinesia were treated from 14 to 18 months with l-dopa. Initial improvements were offset by later development of some generalized dyskinesia and a fluctuating condition labeled akinesia paradoxica. Two general explanations were advanced: progressive loss of catechol-ortho-methyl-transferase and cerebral accumulation of metabolites with resultant monoaminic disequilibrium. The four clinical fluctuation stages observed were: 1) early period temporary dopamine deficiency; 2) later temporary dopamine overdosage; 3) after 6-12 months sharp fatigue and respiratory distress corresponding to diminishing DOPA effectiveness; and 4) intermittent periods of almost complete kinetic system nonreaction.

203495 Thibault, Ph. no address /**Unusual reactions to isoniazid.**/ Reaction inhabituelle de l'isoniazide. Nouvelle Presse Medicale. 2:45-46, 1973.

Secondary effects of isoniazid, a recognized drug for the treatment for mental anorexia, are described. These include irritability, euphoria, insomnia, lack of muscular coordination and sensorial hypersthesis. Antabuse accentuates and provokes idiosyncratic reactions. Monoaminoxidase inhibitors increase the potential of a secondary reaction. Low hydantoin metabolism due to isoniazids in slow-paced systems risks myelopathy and encephalopathy. Likewise cases of hypersensitivity and ictus have been noted.

203546 Crammer, John L.; Rosser, Rachel M.; Crane, Graham. Institute of Psychiatry, London SE4 8AF, England **Blood levels and management of lithium treatment.** British Medical Journal (London). No.5932:650-654, 1974.

The limited value of plasma measurements in the management of treatment with lithium is discussed in the light of the mechanisms of its therapeutic and toxic effects. The plasma level of lithium rises in the 3 to 5 hrs after ingestion of the delayed release tablet and then falls; the shape and height of the curve depend on gastric emptying and drug intake. Patients may be irregular in taking the drug and variable in food intake; and the time of the blood test and this behavior must be considered before changing lithium dosage because of a laboratory result. A lithium tolerance curve may be a safer guide to treatment than single measures. Side-effects of thirst and obesity are discussed. 23 references. (Author abstract modified)

203602 Middelhoff, H. D.; Paschen, K. 732 Goppingen, Privatklinik Christophsbad, Postfach 840, Germany /**The effects of lithium on the EKG.**/ Lithiumwirkungen auf das EKG. Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 7(5):254-264, 1974.

The effects of treatment with lithium on the electrocardiogram (EKG) are examined. An examination conducted before, during and after the administration of lithium salts to normal subjects and patients suffering from a manic-depressive psychosis, showed that comparatively small doses can lead to considerable changes in EKG. The changes include: slight disturbances of sinus rhythm; increased ectopic activity in the form of ventricular and supraventricular extrasystoles in 25% of all subjects; first degree heart block or an intraventricular conduction defect, a disturbance in ventricular depolarization without QRS prolongation; and atypical changes in ventricular repolarization in 40% of the subjects. In general, the changes show a parallel relationship to the height of the serum lithium concentration and appear more distinctly in manic-depressives than in normals. The clinical implications and their consequences for psychiatric therapy are discussed. 45 references. (Author abstract modified)

203741 Dobrzanski, Tadeusz; Fiutowski, Jerzy; Bartoszewski, Jerzy. Jan-Mazurkiewicz-Krankenhaus, Pruszkow/b. Warszawa (VR Polen) /**Studies on antidiuretic activities and on Porter-Silber's chromogen's content in plasma of patients with alcoholic delirium or with acute phenothiazine intoxications.**/ Untersuchungen uber den Gehalt des Plasmas an antidiuretischer Activitat und an Porter-Silber-Chromogenen bei Alkoholdelir und bei akuten Phenothiazin-Intoxikationen. Psychiatrie, Neurologie und medizinische Psychologie (Leipzig). 25(3):153-160, 1973.

Among 98 men suffering from severe alcoholic delirium (98% after a period of forced absolute abstinence (Abs) and the remainder after heavy alcoholic excesses) with signs of reduced corticosuprarenal function, patients (Abs) with undisturbed reaction on an ACTH load and with augmented antidiuretic activity (ADA) before the treatment (with a normalization after 7 days of treatment) were distinguished from patients with reduced reaction on an ACTH load and with normal ADA values. After suicidal phenothiazine intoxications (n=12) a reduction of the plasma's content of Porter-Silber's chromatogens was observed. According to the above-mentioned observations, phenothiazine preparations for the treatment of alcoholic delirium are not recommended. 26 references. (Journal abstract modified)

203784 Kielholz, P.; Hobi, V. Psychiatrische Universitatsklinik Basel, CH-4056 Basel, Switzerland /**The influence of psychopharmaca on the aptitude to drive.**/ Beeinflussung der Fahrtuchtigkeit durch Psychopharmaka. Therapeutische Umschau (Revue Therapeutique) (Bern). 31(9):606-613, 1974.

The alcohol-potentiating effect of psychoactive drugs on driving ability was investigated, and it was found that hypnotics, sedatives and analgesics can interfere with a person's driving ability. Central stimulants, especially amphetamine and methamphetamine, are contraindicated when driving a vehicle, since they may lead to menacing circulatory collapse and to unexpected sleepiness. Psychopharmaceutical drugs, especially those with centrally-sedating spectra, such as neuroleptics, antidepressives and tranquilizers, only adversely affect during aptitude at the start of treatment and thus should be prescribed for initial use only at bedtime. It is recommended that the package folders of drugs indicate possible interference with driving ability. It is found, however, that psychotropic drugs may improve mental disorders, and restore the driving aptitude in patients suffering from fear, depressive states and psychoses. 16 references. (Journal abstract modified)

203882 Schydlo, R. Bonn. 53 Bonn, Adenauer-Allee 119, Univ. Kinderklinik, Germany /**Heavy intoxication as a side-effect of Carbromal in two children.**/ Schwerer Rauschzustand als Carbromal-Nebenwirkung bei zwei Kindern. Klinische Padiatrie (Stuttgart). 186(3):257-258, 1974.

Heavy intoxication as a side-effect of Carbromal in two male children, ages 1 and 3, was studied. It was found that a therapeutic dosage of Ingomidon syrup sufficed to provoke extrapyramidal motor symptoms with restlessness, confusion, vertigo, atactic gait and a tendency to fall. The EEG showed, in the one case, superimposed beta-waves, in the other, slight uncharacteristic general changes. The observed side-effect is attributed to the Carbromal component. 8 references. (Journal abstract modified)

204164 Baldessarini, Ross J. Neuropharmacology Laboratory, Harvard Medical School, Boston, MA 02114 **Tardive dyskinesia: an evaluation of the etiologic association with neuroleptic therapy.** Canadian Psychiatric Association Journal (Ottawa). 19(6):551-554, 1974.

Available literature on the etiology and neuroleptic therapy of tardive dyskinesia is reviewed. Research is advocated on the association of drug effects and the tardive dyskinesia syndrome as well as epidemiological studies in countries where drugs are not generally available. It is suggested that the probability of developing tardive dyskinesia following prolonged exposure to antipsychotic doses of neuroleptic medications is much increased. It is also shown that persistent dyskinesias represent a syndrome or reaction pattern and not necessarily a single disease, and that they can occur in association with senility and many other overt or presumed

states of organic central nervous system disease. 19 references.

204195 van Hoof, F.; Heyndrickx, A.; Timperman, J. Dept. of Toxicology, State University of Ghent, B-9000 Ghent, Belgium **Report of a human fatality due to amphetamine.** Archives of Toxicology (Berlin). 32(4):307-312, 1974.

A pathological report and toxicological examination of an uncommon case of fatal amphetamine poisoning are presented. Amphetamine was quantified in different tissues by thin layer chromatography and spectrophotofluorometry after fluorigenic labeling of amphetamine with 4-chloro-7-nitrobenzo-2,1,3-oxadiazole. The distribution study showed an extremely high concentration of amphetamine in urine and blood; fairly small amounts were found in the contents of the stomach and small intestine. These findings could indicate that the subject had taken amphetamine over a long period and that his death was probably caused by intravenous injection of amphetamine. 6 references. (Author abstract modified)

204233 Johnson, B. E. Dept. of Dermatology, University of Dundee, Dudhope Terrace, Dundee, Scotland **Cellular mechanisms of chlorpromazine photosensitivity.** Proceedings of the Royal Society of Medicine (London). 67(9):871-873, 1974.

In vitro techniques were used to examine cellular mechanisms of chlorpromazine photosensitivity. Preliminary studies indicate that phototoxicity at the cellular level may result from the action of a cytotoxic photoproduct on the plasma membrane, rather than by a complex energy transfer mechanism more usual for phototoxicity. The formation of an hemolytic photoproduct may be a common feature for substances which act clinically as photoallergens. 18 references. (Author abstract modified)

204236 Bant, Wendy. Whiteley Wood Clinic, Woofindin Road, Sheffield, 510 3TL, England **Do antihypertensive drugs really cause depression?** Proceedings of the Royal Society of Medicine (London). 67(9):919-921, 1974.

Mood ratings of 75 new referral hypertensive patients with short duration symptoms were examined to determine whether antihypertensive drugs cause depression. Approximately one-third of patients recorded themselves as depressed on at least one occasion during the followup period, the same incidence as recorded in a group of chronic chest patients. No significant statistical difference was found between the incidence of depression in hypertensive patients on different drug regimes, but the trend was for more patients on adrenergic blocking agents to become depressed than patients on reserpine and methyl dopa. Moreover, more severe depression occurred in patients on the adrenergic blockers than in those on reserpine and methyl-dopa. Depressed patients on adrenergic blockers characteristically suffered chronic type depression, while patients in the reserpine methyl-dopa group recorded both transient and chronic patterns. Results suggest that transient depression may be an amine depletion pattern, but chronic depression is most likely a reflection of the illness itself.

204403 Matussek, N.; Aarons, M. Psychiatrische Klinik der Universitat, 8 Munchen 2, Nussbaumstr. 7, Germany /**Effects of single and repeated administration of maprotiline and its relation to plasma levels in healthy test subjects.**/ Wirkung akuter und chronischer Applikation von Maprotilin und ihre Beziehung zum Plasmaspiegel bei gesunden Versuchspersonen. Arzneimittel-Forschung (Aulendorf). 24(8):1107-1111, 1974.

In a study of plasma levels, maprotiline was administered in a single or in repeated doses, for 6 weeks, in different amounts, to 25 healthy subjects. The investigation showed that the new polycyclic antidepressant drug produced side-effects such as tiredness and dry mouth, similar to those caused by tricyclic thymoleptics. Tiredness and sedation did not lead to a decrease in the concentration performance test. In spite of marked differences in the plasma concentration of the substance at steady state conditions, no significant correlations with the side-effects and test scales were found. 8 references. (Journal abstract modified)

204404 Tolle, R. Psychiatrische und Nervenklinik der Westf. Wilhelms-Universitat, 44 Munster, Roxeler Str. 131, Germany /**Unexpected complications by anticholinergics contained in soporifics and analgesic drugs.**/ Unerwartete Komplikationen durch Anticholinergika in Schlaf- und Schmerzmitteln. Arzneimittel-Forschung (Aulendorf). 24(8):1111-1112, 1974.

Hypnotic and analgesic combination preparations containing anticholinergics were found to cause unexpected complications, including exogenous or symptomatic psychoses. Often these side-effects were unexpected and difficult to diagnose, partly because they occur after a small dose, and partly because the active substances of the combinations are unknown. 9 references. (Journal abstract modified)

204406 Kirkegaard, G.; Kirkegaard, Aage. no address /**Side-effects of methylperone in long-term therapy up to 8 years.**/ Nebenwirkungen von Methylperone bei Dauerbehandlung bis zu 8 Jahren. Arzneimittel-Forschung (Aulendorf). 24(8):1115-1117, 1974.

In a study of its side-effects in long-term therapy, 21 women and 22 men were treated with methylperone for 6 months to 8 years. About 75% were diagnosed as senile psychotics and the rest as schizophrenics, and about 30% were over 70 years old. Before, during, and after treatment, the patients were examined for sedimentation reaction, hemoglobin, leucocytes, plasma creatinine, serum GPT, thymol reaction, serum bilirubin, electrocardiogram, possible ocular changes, and blood pressure. The results reveal no serious side-effects attributable to methylperone. Pathological findings were normalized before the treatment in several cases. 8 references. (Journal abstract modified)

204407 Ziegler, B.; Schneider, E. Abt. fur Klinische Psychiatrie II der Universitat, 6 Frankfurt/M., Heinrich-Hoffmann-Str. 10, Germany /**Treatment of withdrawal symptoms with apomorphine.**/ Behandlung des Entzugsyndroms mit Apomorphin. Arzneimittel-Forschung (Aulendorf). 24(8):1117-1119, 1974.

Twenty-three male drug-dependent patients were treated with apomorphine in a study of withdrawal symptoms. In all cases apomorphine therapy was terminated because of the intensity of withdrawal symptoms, especially severe agitation and dysphoria. These clinical observations correspond to biochemical and neurophysiological examinations which show that withdrawal symptoms are due to an increase of catecholamine and serotonin transmitters. When apomorphine was combined with other drugs, withdrawal symptoms were diminished. 13 references. (Journal abstract modified)

204409 Floru, L.; Floru, L.; Tegeler, J. Psychiatrische Universitatsklinik, Rheinisches Landeskrankenhaus, 4 Dusseldorf, Bergische Landstr. 2, Germany /**Effect of beta-receptor blockers (pindolol and practolol) on lithium-induced tremor -- clinical trial and theoretical considerations.**/ Wirkung von beta-

Rezeptorenblockern (Pindolol und Practolol) auf den lithiumbedingten Tremor -- Klinischer Versuch und theoretische Erwagungen. Arzneimittel-Forschung (Aulendorf). 24(8):1122-1125, 1974.

A clinical attempt to treat lithium-induced tremor in 20 patients with cyclothymic and schizoaffective diseases with two beta-receptor blocking agents, pindolol and practolol, is described. Very good or good results were recorded in more than 66% of the cases, although a certain amount of reversible tachyphylaxia was noted. Pindolol showed a more accentuated and constant positive effect than practolol. An attempt was made to explain the mechanism of lithium-induced tremor and the action of beta-receptor blocking agents on the latter. 40 references. (Journal abstract modified)

204410 Arnold, O. H. Psychiatrische Universitatsklinik Wien, Lazarettgasse 14, A-1090 Vienna, Austria /**Further observations on "automaton-like" existence under long-term lithium therapy.**/ Weitere Beobachtungen zum "automatenhaften Dasein" unter Lithium-Langzeit-Therapie. Arzneimittel-Forschung (Aulendorf). 24(8):1125-1127, 1974.

The behavior of six persons with high social and cultural positions who were continuously treated with lithium is described. For some years the subjects had shown biphasic courses of manic-depressive illness. After about 2 years of lithium treatment, a definite psychic and social adaptation was observed. At the same time a syndrome of distance in emotions, loss of creativity, impoverishment and simplification of behavior and of automatic self-realization was observed. Society defined the patients as being readapted; patients themselves realized a lack of personality and self-identification. 7 references. (Journal abstract modified)

204413 Gabriel, E.; Muller, E.; Presslich, O.; Schuster, P. Psychiatrische Universitatsklinik, Lazarettgasse 14, A 1090 Vienna /**Experimental psychologic and psychophysiologic longitudinal profile studies on depressive patients under thymoleptic medication.**/ Experimentalpsychologische und psychophysiologische Langsschnittuntersuchungen an depressiven Patienten unter thymoleptischer Medikation. Arzneimittel-Forschung (Aulendorf). 24(8):1131-1133, 1974.

Longitudinal studies under thymoleptic medication are presented, and the acoustic activation in patients suffering from endogenous depression equal with respect to descriptive psychopathology was examined. Significant differences in psychological test scores measuring deviations in mental state define the dates of polygraphic registration of some physiological parameters. 16 references. (Journal abstract modified)

205288 Solomon, Kenneth; Vickers, Raymond Dept. of Psychiatry, Albany Medical College, Albany, NY **Dysarthria resulting from lithium carbonate: a case report.** Journal of the American Medical Association. 231(3):280, 1975.

A case history is presented which illustrates dysarthria resulting from lithium carbonate. The slurred speech occurred as a solitary symptom of lithium carbonate administration at maintenance dosage in a 70-year-old male. The patient had no concomitant symptomatic medical conditions and was receiving no other medication. His dysarthria was unaccompanied by any other symptoms of a toxic reaction. It is suggested that physicians might warn their elderly patients about possible difficulties with the police since their speech patterns may resemble those of an alcoholic. 3 references.

205315 Black, Dora; Woollacott, Susan. Hospital for Sick Children, Great Ormond Street, London, WC1 N3JH England **Acute toxic psychosis in two children treated with benzhexol hydrochloride (Artane).** British Journal of Psychiatry (London). 125:483-484, 1974.

Case reports and discussions are presented of two children seen at an inpatient psychiatric unit who developed acute psychotic reactions when treated with benzhexol hydrochloride (Artane) given to prevent extrapyramidal side-effects. In both cases, complete recovery occurred rapidly when benzhexol was discontinued. 4 references. (Author abstract modified)

205594 Bastecky, J.; Gregova, L. Institute of Psychiatry, 18103 Prague 8-Bohnice, Czechoslovakia **Priapism as a possible complication of the chlorpromazine treatment.** Activitas Nervosa Superior (Praha). 16(3):175, 1974.

At the 16th Annual Psychopharmacological Meeting, a case of a male patient, 35-years-old, single, a tractor driver, who since 1965 had been four times admitted to mental hospitals for manic phase of manic-depressive disease was reported. He was treated with different neuroleptic drugs (chlorpromazine, reserpine and oxyprothepine) each time, 3 months on an average. During the last admission to the Institute of Psychiatry (1973) chlorpromazine was administered in a dose of 500 mg daily. After 20 days of the treatment priapism occurred. The patient was transferred to the urology department where a punction of the corpora cavernosa was performed. Thrombophlebitis of the corpora cavernosa and other symptoms of inflammation were observed. The patient was discharged without any symptoms. It was concluded that the priapism was of unknown etiology as no internal or external factors were involved. Chlorpromazine was seen as the only possible cause. 7 references.

205595 Kopriva, K.; Frantik, E.; Horvath, M. Institute of Hygiene, Praha 10, Srobarova 48, Czechoslovakia **Pentobarbital effect on performance in monotonous conditions not prevented by compensatory effort.** Activitas Nervosa Superior (Praha). 16(3):176-178, 1974.

At the 16th Annual Psychopharmacological Meeting, a study of the pentobarbital effect on performance in monotonous conditions not prevented by compensatory effort was reported. Pentobarbital had no effect on the instruction for compensation on errors of omission. With regard to errors of commission the situation was reversed; no drug effect could be evidenced while the influence of the instruction was apparent in the sense that subjects who were given positive instruction for compensation had significantly more false positive reactions. The increase in errors of omission under the effect of pentobarbital coincides with the anticipated inhibitory action of the drug. It is interesting that this effect was not in the least affected by the instruction for compensation. The fact that the instruction influenced errors of commission indicates that the subjects did not simply ignore it. 3 references.

205596 Bauer, M.; Molcan, J. Sasinkova ul. 4, 884 24 Bratislava, Czechoslovakia **Volatile solvent addiction and traffic safety.** Activitas Nervosa Superior (Praha). 16(3):178-179, 1974.

A paper presented at the 16th Annual Psychopharmacological Meeting, examines the effects of trichloroethylene and toluene addiction on traffic safety. Results indicate that the inhalation of volatile solvents which, unfortunately has a rising tendency, represents a further addition to the adverse factors

endangering traffic safety. It is clear that for evidencing the described drugs, reliable and rapid analytic methods are available which can be used preventively or in the complex assessment of the cause of the traffic accident.

205597 Nemec, J. Branch Institute, Rosice nad Labem, Gzechoslovakia Czechoslovakia **Cardiotoxic effects of tricyclic antidepressants imipramine, amitriptyline and dosulepin (Prothiaden Spofa) in an acute experiment in rats.** Activitas Nervosa Superior (Praha). 16(3):182-183, 1974.

A paper presented at the 16th Annual Psychopharmacological Meeting, describes an acute experiment in which the cardiotoxicity of imipramine, amitriptyline, and dosulepin in rats were compared. After single intravenous doses of all of the drugs tested, the PR, QRS, and QT intervals were found to be prolonged. During slow intravenous infusion of 0.25% and 0.5% solutions, increasing bradycardia was observed. As the dose administered increased, there occurred A-V blockage, dropped nodal beats, and ventricular extrasystoles. In young rats, all three drugs exhibited approximately the same toxicity; in old rats, dosulepin and imipramine appeared to be less toxic than amitriptyline. In a model of emetine-induced cardiopathy the cardiotoxicity of all three drugs increased. Premedication with digitoxin enhanced the cardiotoxicity of the drugs tested only statistically, not significantly. In these tests, imipramine and dosulepin likewise appeared to have lesser cardiotoxicity than amitriptyline. In a model of coronary ischemia even high doses of the antidepressants elicited no major disturbances of the heart rhythm. 5 references.

16 METHODS DEVELOPMENT

199214 Devriendt, A.; Weemaes, I.; Jansen, F. H. Dept. of Pediatrics, St. Elisabeth Ziekenhuis, Turnhout, Belgium **Colorimetric, ultraviolet spectrophorometric, and spectrophotofluorometric determination of doxepin and some of its metabolites in serum and in urine.** Arzneimittel-Forschung (Aulendorf). 23(6):863-867, 1973.

Methods for the determination of 11-dimethylaminopropylidene-6H-dibenz(b,e)oxepine (doxepin) in the body fluids and the urine, as well as of some of its metabolites are proposed. Techniques reviewed cover colorimetric methods, including a reaction with tetra-iodo-fluoroscein and one with methyl orange, an ultraviolet spectrophotometrical method, a spectrofluorometric method, involving a tetra-iodo-fluorscein reaction, and finally a method to quantify the various metabolites excreted in the urine. 10 references. (Author abstract modified)

200737 de Silva, J. Arthur F.; Bekersky, Ihor; Puglisi, Carl V. Department of Biochemistry and Drug Metabolism, Hoffmann-La Roche, Inc., Nutley, NJ 07110 **Spectrofluorodensitometric determination of flurazepam and its major metabolites in blood.** Journal of Pharmaceutical Sciences. 63(12):1837-1841, 1974.

The spectrofluorodensitometric determination of flurazepam and its major metabolites in blood is discussed. The spectrofluorodensitometric assay for the determination of flurazepam and its major metabolites involves selective extraction of flurazepam and its major metabolites into ether and hydrolysis in acid to their respective benzophenones, which are cyclized in dimethylformamide-potassium carbonate to their respective 9-acridanone derivatives and separated by thin layer chromatography (TLC). The fluorescence of the 9-acridanones is measured directly on the chromatoplate, using a scanning TLC analyzer in the reflectance mode. The limits of detection of the assay are 0.5ng-1.0ng of each compound/ml of blood using a 4 ml specimen/analysis. 23 references. (Author abstract modified)

200740 Walle, Thomas. Department of Pharmacology, Medical University of South Carolina, Charleston, SC 29401 GLC **determination of propranolol, other beta-blocking drugs, and metabolites in biological fluids and tissues.** Journal of Pharmaceutical Sciences. 63(12):1885-1891, 1974.

A highly sensitive and specific electron capture gas liquid chromatography (GLC) method was developed for beta blocking drugs, including propranolol, oxprenolol, alprenolol, pronethalol, dichloroisoproterenol, practolol, and sotalol, and several of their metabolites. The drugs are separated and detected as their trifluoroacetyl derivatives. Minimum detectable amounts ranged from 0.1pg to 1.1pg. Propranolol was extracted from plasma by either a single or a back extraction procedure, with oxprenolol as the internal standard. The minimum detectable concentration was 0.1ng/ml plasma. Applications of this method demonstrated quantitatively detectable plasma propranolol levels 24 hours after a small (.05mg/kg) intravenous dose. Accurate plasma determinations could be made in patients receiving numerous other drugs. The method was shown to be applicable to propranolol and two metabolites, 1-(alpha-naphthoxy)-2,3-propylene glycol and N-desisopropylpropranolol, in tissue. 18 references. (Author abstract modified)

203845 Helmchen, H.; Hippius, H.; Kanowski, S.; Mauruschat, W.; Rosenberg, L. Psychiatrische Klinik II der Freien Universitat Berlin, 1 Berlin 19, Nussbaumallee 36, Germany **/Multidimensional psychopharmacotherapeutic trials with the neuroleptic Perazine. 7. Communication: Methodological outcome./** Multidimensionale pharmakopsychiatrische Untersuchungen mit dem Neuroleptikum Perazin. 7. Mitteilung: Methodologische Ergebnisse. Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 7(1):58-64, 1974.

A broad discussion on the methodological aspects of studies on the effects of the drug Perazine is presented. A system of drug evaluation in psychiatry is suggested, and the formal criteria of the various variables are systematically specified. Methods for analysis and interpretation of the course of treatment are summarized. Organizational problems in multidimensional designs of investigations are noted. The methodological consequences of the incomplete data matrix are discussed in detail. 4 references. (Author abstract modified)

204395 Aschoff, J. C.; Becker, W.; Weinert, D. Abt. f. Neurologie der Universitat Ulm, Nervenzentrum, 7900 Ulm, Steinhovelstr. 9, Germany **/Computer-nystagmography, a new method of determining changes in vigilance as a response to psychotropic drugs./** Computer-Nystagmographie als neue Bestimmungsmethode von Vigilanz und Reaktionsverhalten unter Psychopharmaka. Arzneimittel-Forschung (Aulendorf). 24(8):1085-1087, 1974.

For evaluating precisely reactions to drugs or alcohol, an on-line computer program was developed by which 500 saccadic eye movements, registered by means of electronystagmography, were analyzed for their maximum velocity, accuracy, and reaction times. A new thymoleptic/neuroleptic drug, N-((1-ethylpyrrolidin-2-yl)-methyl)-2-methoxy-5-sulfamoyl-benzamide (known as sulpiride or Dogmatil) tested with this new method showed no influence on velocity and reaction times and may even enhance the accuracy of saccadic eye movements. It is considered safe in normal situations. 7 references. (Journal abstract)

204401 Slanska, J. Pharmakologisches Institut, Hygienisch-medizinische Fakultat, Karls-Universitat, Prague, Czechoslovakia /**Aspects of using psychological methods in studying the effects of psychotropic drugs.**/ Aspekte der Benutzung psychologischer Methoden bei der Erforschung von Psychopharmakawirkungen. Arzneimittel-Forschung (Aulendorf). 24(8):1102, 1974.

On the basis of experiments with a low dose of physostigmine (Phs) in 14 undergraduate subjects, some aspects of psychological methodology are demonstrated which differentiate the drug's action more accurately. An important factor is the time schedule of drug administration and administration of psychological tests. Phs had different effects when administered in the acquisition or consolidation phases. A further parameter under consideration is personality; Phs influenced labile subjects differently from stable ones. Results are discussed in terms of long-term studies. 5 references. (Journal abstract modified)

205522 Fink, Max. Stony Brook, NY **Drugs, EEG and behaviour: EEG profiles and bioavailability measures for clinical psychopharmacology.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 34(7):754, 1973.

A paper presented at the 8th International Congress of Electroencephalography and Clinical Neurophysiology describes electroencephalogram (EEG) profiles and bioavailability measures for clinical psychopharmacology. These methods are used to define clinical applications for new psychoactive drugs in phase 1 pharmacology. Applications in studies of doxepin, thiothixene, fenfluramine, cyclazocine and numerous numbered compounds were demonstrated on male volunteers. The techniques are based on period and power spectral density analyses of continuous postdrug records. (Author abstract modified)

17 MISCELLANEOUS

198105 Cisin, Ira H.; Parry, Hugh J.; Manheimer, Dean I.; Mellinger, Glen D. George Washington University, Washington, DC **Patterns of drug acquisition and use.** Psychopharmacology Bulletin. 10(2):71, 1974.

The extent and character of psychotherapeutic drug use in the U.S. are being studied. Subjects for the validation study were persons who had filled prescriptions for selected types of drugs. Of those interviewed, 22% had used a medically-prescribed psychotherapeutic drug during the year prior to interview. Prevalence of use of the medically-prescribed drugs was twice as high among women as among men and was appreciably higher among older than among younger persons. The number of persons who have experienced relatively severe life crises or emotional distress is considerably greater than the number using medically-prescribed psychotherapeutic drugs. Majority attitudes regarding use of psychotherapeutic drugs are generally conservative, even among persons who use them. Over the counter (OTC) drug use showed no sex bias, was most prevalent in the 18 to 30 age group, and was much less regular than prescription drug use. (Journal abstract modified)

198107 Overall, John E. University of Texas Medical Branch, Galveston, TX **Psychopharmacology computer research.** Psychopharmacology Bulletin. 10(2):72-73, 1974.

A computer laboratory is described, which was established to facilitate the development and use of quantitative techniques for evaluation and classification of psychiatric patients and to apply these techniques in clinical drug research with the aim of determining the most effective treatment for each type of patient. The subjects are psychiatric inpatients and outpatients. Tricyclic antidepressants were found superior to other classes of drugs for retarded depressions. Age, sex, and previous course of illness appeared drug specific in their relations to outcome. Eight phenomenological profile patterns have been found to account for most patients in both American and French psychiatric populations. (Journal abstract modified)

198327 Bohacek, N. Department of Psychiatry with the Mental Health Center, Medical Faculty, University of Zagreb, Yugoslavia /**Social aspects of psychopharmacotherapy.**/ Socijalno znacenje psihijatrijske farmakoterapije. In: Persic, N., Socijalna Psihijatrija. Zagreb, Pliva, 1971. 823 p. (p. 494-496).

Social aspects of psychotropic drug therapy are examined. Psychiatric institutions which used to receive psychiatric patients for permanent hospital care have changed into institutions receiving the patients for short-term stays after which outpatient treatment and supervision are possible. The more human atmosphere in psychiatric hospitals as well as more human attitudes toward psychiatric patients in society are results of psychopharmacotherapy. Since maintenance therapy with psychotropic drugs is available in outpatient conditions, rehabilitation and resocialization is more adequate and more rapid. 2 references. (Journal abstract modified)

198393 Rogina, V. Vrapce Psychiatric Hospital, Zagreb, Yugoslavia /**Sociopsychiatric aspects of psychopharmacology.**/ Socijalnopsihijatrijsko znacenje psihofarmakologije. In: Persic, N., Socijalna Psihijatrija. Zagreb, Pliva, 1971. 823 p. (p. 801-804).

Resocialization processes and techniques are discussed as key points of interdependence in social psychiatry and psychopharmacology. A rational combination of techniques is the treatment of choice. A rational administration of psychotropics should help ease pathological tensions and anxiety, but it should not deprive man of some of his vital existential potentialities. 2 references. (Journal abstract modified)

198823 Greenblatt, David J.; Shader, Richard I. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **Rational use of psychotropic drugs -- III. Major tranquilizers.** Journal of the Maine Medical Association. 65(10):251-256, 260, 1974.

The attributes and application of major tranquilizers are discussed. Three important categories of clinically useful major tranquilizers are: the phenothiazines, the butyrophenones, and the thiozanthenes. They are primarily used in relatively high doses as antipsychotic agents in psychiatry. Most major tranquilizers appear to have similar efficacy in the treatment of schizophrenia, but they differ considerably in their additional or secondary pharmacologic properties, side-effects, and toxicity. The pharmacologic properties and potentially toxic effects discussed include nonspecific sedation, adrenergic antagonism, antiemetic effects, extrapyramidal symptoms, cardiac toxicity, temperature regulation, and cholinergic blockade. Major tranquilizers are considered for clinical use in nonpsychiatric conditions such as confusion and delirium, alcohol withdrawal, amphetamine toxicity, nausea and vomiting, hyperpyrexia, and intractable hiccough. 109 references.

199636 Jefferson, James W. Dept. of Psychiatry, Univ. of Wisconsin, 1300 University Ave., Madison, WI 53706 **Beta-adrenergic receptor blocking drugs in psychiatry.** Archives of General Psychiatry. 31(5):681-691, 1974.

The utility and application of beta-adrenergic blocking drugs in psychiatry are discussed. Beta-adrenergic blocking drugs have been employed in a variety of psychiatric conditions with variable success. The beta blockers appear to have an antianxiety action that is best established in the treatment of psychocardiac disorders but is less well defined with regard to other anxiety related conditions. A paucity of studies comparing them with conventional anxiolytic drugs is one reason for not presently recommending their widespread use. As antipsychotic agents, the beta blockers have shown promise in studies that, at present, must be considered preliminary, while they clearly have potential as tools for investigating the neuropharmacology of psychosis. If future resarch with these compounds proceeds in an organized, scientific fashion, the beta-adrenergic receptor antagonists will quite likely become established as effective psychotherapeutic drugs. 123 references. (Author abstract)

199907 Higuchi, Masamoto. Jikei University, Japan **Psychotherapy and drugs from the standpoint of internal medicine.** Practice and Theory of Psychotherapy (Tokyo). 5(2):29-35, 77, 1974.

The use in Japan of psychotropic drugs in internal medicine and in psychotherapy is reported. At present, it is not rare for a psychotropic drug, especially a minor tranquilizer, to be substituted for psychotherapy. Although psychotherapy and the treatment with psychotropic drugs make up for each other, it

is suggested that the latter be subordinate to the former in the treatment of neuroses or psychosomatic diseases, except for mild depression, which can be treated in the sphere of internal medicine. The importance of careful prescriptions and a mutual understanding of the treatment between the patient and the therapist is emphasized. 7 references. (Journal abstract modified)

200231 Behavioral Sciences Tape Library, c/o Sigma Information, Inc., 240 Grand Avenue, Leonia, NJ 07601 (201-947-4154) BST (S)$7.95 ea. **Pharmacotherapy of the Psychoses.** AT 1 7/8 IPS cassette 60 min ea., 1974.

New pharmacological solutions to problems in the management of stubborn psychoses are presented by Dr. Aaron D. Mason of Eastern State Hospital, Lexington, Kentucky. The individual tape titles are: 1) The use of the antipsychotic agents; 2) The use of the antipsychotic agents (cont'd); and 3) The side-effects of antipsychotic agents and their treatment, lithium therapy, pharmacotherapy in the elderly.

200438 no author. no address **Suit against recommending doctor and psychiatrist -- rejected. Stovall v. Harms, 522 P.2d 353, (Kansas) Supreme Court of Kansas. May 11, 1974.** Mental Health Court Digest. 18(5):6, 1974.

In Stoval v. Harms, the Supreme Court of Kansas rejected a suit for recovery of damages for personal injuries received in an automobile collision. The suit claimed that the accident was the result of negligence on the part of a physician and a psychiatrist in prescribing drugs to the plaintiff. The Court ruled that it was not reasonable that the doctrine of informed consent be interpreted to require a general practitioner, referring his patient to a psychiatric specialist, to advise the patient of risks and dangers incident to the psychiatric treatment (as contended by plaintiff) in the absence of unusual circumstances.

200447 Sakai, Masao; Moriguchi, Yoshiko; Saito, Atsushi. Department of Neurology and Psychiatry, Yokohama City University School of Medicine, Japan **A survey of drug treatment in psychiatry: special emphasis on inpatients on medical welfare supported by Yokohama City.** Clinical Psychiatry (Tokyo). 16(7/8):651-659, 1974.

The status of psychopharmacological treatment given to 1,320 hospitalized patients who were receiving medical financial assistance from Yokahama City was studied, based on doctors' bills submitted to the City during a 1-month period. It was found that 60% of the patients had schizophrenia, and the others, toxic psychosis, psychopathic personality, mental retardation, vascular psychosis, senile psychosis, and epilepsy. Psychopharmacological treatment was being administered to 95% at an average rate of 2.9drugs per patient. An overuse of psychotropic and antiparkinson drugs is indicated. 11 references.

200980 Richardson, J. Steven. Department of Pharmacology, College of Medicine, University of Saskatchewan, Saskatoon, Canada S7N OWO **Basic concepts of psychopharmacological research as applied to the psychopharmacological analysis of the amygdala.** Acta Neurobiologiae Experimentalis (Warsaw). 34(4):543-562, 1974.

Basic concepts of psychopharmacological research as applied to the psychopharmacological analysis of the amygdala are discussed. Recent data indicating an extensive interaction between the various neurotransmitters on a cellular and even synaptic level suggest that interpreting the behavioral effects of drugs in terms of only one neurotransmitter is a potentially misleading oversimplification. Perhaps, rather than the action of a single neurotransmitter, it is the balance between neurotransmitter systems that determines behavior. Because of its rich innervation by noradrenaline, dopamine, serotonin and acetylcholine synapses, the amygdala is ideally suited for monitoring the balance between these neurotransmitters and for altering maladaptive behavior based on fluctuations in neurotransmitter balance. 141 references. (Author abstract modified)

201241 Kazamatsuri, Hajime; Ayd, Frank J., Jr. Dept. of Neuropsychiatry, Teikyo University, Japan **The art of psychopharmacology.** Clinical Psychiatry (Tokyo). 16(7/8):645-651, 1974.

The correct methodology in practicing psychopharmacology is discussed. Before prescribing any psychotropic drugs, psychiatrists should diagnose the psychiatric and physical condition of their patients, and take the drug history of the patients and the families. The danger of polypharmacy should be carefully avoided. Types of psychotropic drugs and their pharmacological effects and side-effects are also discussed. 5 references.

201270 Silverstone, Trevor; Turner, Paul. no address **Social and psychological aspects of medical practice: drug treatment in psychiatry.** London, Routledge and Kegan Paul, 1974. 223 p. L4.00.

General principles of psychopharmacology are discussed and methods of studying drug effects are reviewed. Social and psychological aspects of drug taking and drug abuse are considered. Clinical use of pharmacological agents for various types of psychiatric syndromes are explained.

202029 Simon, Pierre; Colonna, Lucien. no address /**To better know and better prescribe psychotropic drugs.**/ Mieux connaitre et mieux prescrire les psychotropes. Edite par un Laboratoire, 1973.

A manual on understanding and prescribing psychotropic drugs is presented. The drugs are presented in seven groups: neuroleptics, imipramine-like antidepressants, monoaminoxidase inhibitors, tranquilizers, amphetamines, psychostimulants, and psychodysleptics. Each group of psychotropic drugs is reviewed according to its therapeutic effect, the course of treatment, secondary effects and their correction, and the treatment of acute intoxication. The differences between the imipramines and the monoaminoxidase inhibitors are clearly outlined. The final section of the manual is devoted to choosing the type of chemotherapy to be used in the major psychiatric syndromes.

202161 Yamashita, Itaru. Department of Neuropsychiatry, Hokkaido University, Japan **Anxiety and activities of cyclic adenosine monophosphate phosphodiesterase.** Igaku no Ayumi (Tokyo). 83(8):526-527, 1972.

An article, "Cyclic Adenosine Monophosphate Phosphodiesterase in the Brain: Effect on Anxiety," by Beer, is reviewed. Meprobamate and pentobarbital were noted to have remarkable antianxiety action clinically, but the reasons why these drugs show no prohibition on cyclic adenosine monophosphate phosphodiesterase activity are not handled. Lack of consideration that such drugs as phenobarbital, haloperidol, morphine and doxepin which have strong antianxiety action but do not influence cyclic adenosine monophosphate phosphodiesterase activity, is deplored.

Failure to comprehend that such drugs as theophylline, caffeine, and theobromine, which have almost no antianxiety action, influence prohibition of cyclic adenosine monophosphate phosphodiesterase activity is also noted. 1 reference.

202304 Gross, Franz. Department of Pharmacology, University of Heidelberg, FRG **The future: hopes and fears.** World Health. April:28-32, 1974.

The expectations of new chemotherapy and the risks involved are presented. The most spectacular advances so far have been made in the treatment of infectious and parasitic diseases. On the other hand, little progress has been made in antiviral chemotherapy. For instance, it is not expected that a cure for cancer will be forthcoming in the near future. The use of drugs for cardiovascular disease treatment and in psychotherapy is reviewed.

202380 Schildkraut, Joseph J. Dept. of Psychiatry, Massachusetts Mental Health Center, Harvard Medical School, Boston, MA **The current status of biological criteria for classifying the depressive disorders and predicting responses to treatment.** Psychopharmacology Bulletin. 10(1):5-25, 1974.

In a summary of proceedings of a study group which convened at the 1972 annual meeting of the American College of Neuropsychopharmacology, an evaluation of the current status of biological criteria for classifying the depressive disorders and predicting differential response to pharmacotherapy is reported. An overview of literature emphasizes biological criteria related to biogenic amine metabolism. Consideration is also given to criteria related to other areas of biology, including: the physiology of sleep, thyroid function and physiology, neuroendocrinology, electrolyte metabolism and physiology, and genetics. Criteria based on a number of pharmacological tests are also reported. 135 references.

202458 Lapierre, Y.-D. Hopital Pierre-Janet, Hull, Quebec, Canada /**Sedatives, hypnotics and tranquillizers.**/ Sedatifs, hypnotiques et tranquillisants. Vie Medicale au Canada Francais (Quebec). 3(6):605-609, 1974.

A general review of available hypnotics, sedatives and tranquillizers is presented and their indications and counterindications are emphasized. Minor tranquillizers (thymoleptics) considered include: propanediol derivatives, benzodiazepines, antihistamines, anticholinergics, barbiturates and bromines. Nonbarbituric hypnotics discussed are alcohols, piperidinediones, carbamates, chloral hydrate, cyclic ether, methaqualone and benzodiazepines. This classification system for practical use is made in view of increased prescription, acceptance and usage of these drugs. (Author abstract modified)

202500 Koike, Kiyoyuki. Takachaya Hospital, Komoricho, Takachaya, Tsu, 514, Japan **The present conditions of psychopharmacological treatment for children in Japan: opinions from thirty-seven well-known child neuropsychiatrists and neuropsychiatric pediatricians.** Japanese Journal of Child Psychiatry (Tokyo). 14(4):200-217, 1973.

Professional opinions on the present conditions of psychopharmacological treatment for children in Japan are reported. Drug therapy was reported for about 50% of the outpatients and for 80% of the inpatients of psychiatric clinics and 20% of the outpatients and 6% of the inpatients of pediatric clinics. Main target symptoms of drug therapy were: hyperkinetic and destructive behaviors, sleep disturbance, anxiety, hallucination and delusion, depression and enuresis. Most of the drugs used were tranquilizers. Psychiatrists generally used more drugs than pediatricians did. Most of the doctors questioned indicated the need for a reexamination of the use of drug therapy. 3 references. (Journal abstract modified)

202783 Lader, Malcolm. Institute of Psychiatry, University of London, London, England **The peripheral and central role of the catecholamines in the mechanisms of anxiety.** International Pharmacopsychiatry (Basel). 9(3):125-137, 1974.

The peripheral and central role of catecholamines in the mechanisms of anxiety were examined. Anxiety is both an emotional state and a personality trait and may be either normal or pathological. The physiological changes of anxiety can be induced by sympathomimetic agents but the accompanying psychological changes may not be typical of anxiety. Conversely, the physiological concomitants can be attenuated using beta-adrenoceptor blocking agents although psychic anxiety may be only partly ameliorated. The central biochemical aspects of anxiety are poorly understood. Catecholamines rather than indole amines appear to be involved in stress reactions. The locus coeruleus, a structure in the brainstem projecting widely to the cerebral cortex, has mainly adrenergic neurones and can be postulated to play a key role in the genesis of anxiety. In the treatment of anxious patients a combination of a central anxiolytic such as a benzodiazepine and a peripheral beta-blocker such as propranolol may be most efficacious. 38 references. (Author abstract)

202797 Whitlock, F. A.; Price, J. Department of Psychiatry, University of Queensland, Brisbane, Queensland, Australia **Use of beta-adrenergic receptor blocking drugs in psychiatry.** Drugs (Basel). 8(2):109-124, 1974.

The value of propranolol or other beta-blocking drugs in psychiatry was examined. Studies on anxiety for the most part have been of relatively short duration and, although some workers have claimed benefits for propranolol administration, more recent and better controlled trials have failed to demonstrate advantages over placebo treatment. The possibility remains that control of the autonomic symptoms associated with anxiety to some degree diminishes the patient's distress in the face of an unpleasant affect. Hence there may be merit in the opinion that the autonomic symptoms appear to act as signals which are interpreted as warnings of impending danger. Such activation in its turn results in the psychological experience of anxiety. 64 references. (Author abstract modified)

202861 Blum, Richard H.; Bovet, Daniel; Moore, James. no address **Controlling drugs: international handbook for psychoactive drug classification.** San Francisco, Jossey-Bass, 1974. 378 p. $25.00.

Problems in the classification of drugs under the Controlled Substances Act of 1970 are discussed. The uncertainty of drug classification, alternatives based on the criminal law, evaluation of control systems, and the value judgment basis of policy formulation are considered.

202865 Heimann, H. Psychiatrische Klinik der Universitat Lausanne, Hopital de Cery CH-1008 Prilly, Switzerland /**Assay of psychotropic substances in man.**/ Prufung psychotroper Substanzen am Menschen. Arzneimittel-Forschung (Aulendorf). 24(9):1341-1346, 1974.

The problems encountered in a scientific investigation of the effects of psychotropic compounds in man are elucidated on the basis of five main factors that govern such effects at the behavioral level. Consideration is given to the differing degrees of incontestability with which these factors and as-

sociated phenomena can be comprehended. Examination strategies designed to analyze the influences of various factors are discussed, and it is demonstrated that several test programs are necessary to distinguish the effects of psychotropic compounds in man, or to grasp the influence of the twin factors, personality and situation, as modifiers of the effect. The discussion concludes with a psychophysiological model for assaying psychotropic compounds which explains the inconsistency of certain psychological test results in the investigation of psychotropic effects. 15 references. (Journal abstract modified)

202883 Raft, David; Gomez, Raoul; Ewing, John A. Dept. of Psychiatry, Univ. of North Carolina School of Medicine, Chapel Hill, NC 27514 **The pentobarbital test dose for depressant drug dependence: a re-evaluation in terms of alcohol consumption.** Journal of Nervous and Mental Disease. 159(5):366-370, 1974.

The single dose pentobarbital test described by Ewing and Bakewell for depressant drug dependence was evaluated in a nonpatient population. Twenty-four healthy young college student volunteers were studied. Subjects were given 200mg of pentobarbital or placebo, and mental status and physiological signs were evaluated in 1 hour. Serum pentobarbital levels were studied hourly. Twelve subjects had a history of moderately heavy alcohol consumption while 12 were abstainers. None was a drug abuser. A history of moderately heavy alcohol intake was particularly associated with resistance to the effects of pentobarbital consonant with current concepts of cross-tolerance due to induction of liver enzyme systems. It is concluded that a single 200mg pentobarbital test can be used to screen out subjects who fall asleep, but that inferences as to tolerance to barbiturates or minor tranquilizers should be drawn cautiously for those who react to the test otherwise. Continuing test doses of pentobarbital offer a more reliable diagnosis in doubtful cases. 8 references. (Author abstract)

202923 AMA Committee on Alcoholism and Drug Dependence. 535 N. Dearborn St., Chicago, IL 60610 **Barbiturates and barbiturate-like drugs: considerations in their medical use.** Journal of the American Medical Association. 230(10):1440-1441, 1974.

Considerations in prescribing barbiturates and barbiturate-like drugs are reported. Areas discussed include abuse potential, dependence liability, medical indications, and medical hazards. Major factors to consider include the severity of symptoms in terms of the patient's ability to accommodate them, the patient's reliability as a drug taker, and the dependence liability of the drug itself. Other hazards in the prescription and use of barbiturates are discussed, and 10 points to remember when administering or prescribing the drugs are included.

203496 Hodel, Jo. no address **/Treatment of sexual delinquency with Androcur (cyproterone acetate)./** Traitement des delinquances sexuelles avec l'Androcur (cyproteronacetate). Medecine et Hygiene (Geneve). 31:192, 1973.

The use of Androcur (cyproterone acetate) to treat criminals guilty of sexual offenses is discussed. Its use for treatment of sexual deviation has been shown by recent study 70-85% effective by inducing serious inhibition of sexuality, reducing sexual impulse much as castration would. An injectable version has been developed for use weekly to biweekly, and which has an action latency period of 2 to 4 weeks. After treatment stops, behavior patterns often change as the patient has in the interim discovered other outlets for his sexual energy.

204306 Parish, P. A.: Williams, W. M.; Elmes, P. C. no address **The medical use of psychotropic drugs.** London, Longman Group, Journal Division, 1972. 80 p. L1.75.

Medical uses of psychotropic drugs are discussed. Differences of opinion in regard to the abuse potential of the benzodiazepines are presented. The extent and nature of medicine taking in specific groups are focused on. Adverse reactions to psychotropic drugs are covered.

204426 Kato, Kiyoshi. National Kyoto Hospital, Kyoto, Japan **Significance of psychotherapy used with drugs.** Practice and Theory of Psychotherapy (Tokyo). 5(2):1-6, 75, 1974.

The role of the Medusa complex in the patient's psyche and body is discussed to clarify the psychopharmacological dynamics of psychotherapy combined with the use of psychotropic drugs. Two patients, one neurotic and the other schizophrenic, are used as examples. In the mentally ill, the Medusa symbol causes not only threatening stress in the patient's psyche, but also abnormal metabolic changes in the body. Drugs counteract the physiologically toxic effects of the Medusa symbol and transform it into other symbols such as a jellyfish octopus or cuttlefish. With the help of drugs, patients can symbolically behead Medusa, while the therapist assumes the role of the mirror. It is suggested that the examples presented offer important cues in pharmacotherapy. 9 references. (Author abstract modified)

204427 Nishizono, Masahisa. Fukuoka University School of Medicine, Japan **Drugs and pharmacotherapy.** Practice and Theory of Psychotherapy (Tokyo). 5(2):7-16, 75-76, 1974.

Pharmacotherapy, in which psychotherapy and drug therapy are combined, is discussed. Psychiatric disorders have a somatogenic or psychogenic origin, but it is felt that their essential nature is psychophysiological. In cases which are unresponsive to either psychotropic medication or to psychotherapy, there are strong psychophysiological homeostatic defenses which resist both medication and psychotherapy. Combining these therapies in pharmacotherapy is considered helpful in such cases. Two kinds of pharmacotherapy have been developed. One sedates deep-seated anxiety in the patient and then treats his problems with psychotherapy. The other uncovers the patient's anxiety by psychotherapy or mood-regulating drugs. The aggressive and impulsive attitudes in patients are often disclosed by the latter method. 17 references. (Author abstract modified)

204468 Christiani, E.; Stubing, G. no address **/Drug abuse and drug dependency. A compendium for medical doctors./** Drogenmissbrauch und Drogenabhangigkeit. Ein Compendium fur Arzte. Koln, Deutscher Arzte Verlag, 1972. 120 p. 9 DM.

A reference manual geared to the needs of the medical practitioner treating drug addiction is presented. Practical aspects of drug treatment are stressed. Various forms of addiction are reviewed, along with the types, origins, and indications for use of various therapeutic drugs. The problem of handling youthful addicts is examined from a psychological viewpoint.

204478 Zauner, Johann. 3405 Tiefenbrunn, Niedersachsisches Landeskrankenhaus, Germany **/Psychopharmaceutics and clinical psychotherapy./** Psychopharmaca und klinische Psychotherapie. Zeitschrift fur Psychosomatische Medizin und Psychoanalyse (Gottingen). 20(2):138-147, 1974.

The thesis is presented that clinical psychotherapy should not be considered as a specialized discipline until new, analytically-oriented forms of treatment, in the sense of applied psychoanalyis, are developed. Integration of other therapeutic methods, such as pharmacotherapy, into the overall plan of psychotherapeutically oriented treatment is advocated. The use of medication is seen as one aspect of the physician-patient relationship, the dynamics of which can be discussed and rendered additionally useful in the course of therapy. It is important to realize that feelings of transference and countertransference can play a role in the prescription and efficacy of the medication. Three basic areas of application have emerged for psychotherapy: during preliminary treatment; supportively in the course of treatment, should an internal threat arise; and in the evaluation of social experiences such as extraclinical work or study experiments. 10 references. (Journal abstract modified)

204851 Greenblatt, David J.; Shader, Richard I.; Koch-Weser, Jan. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **Flurazepam hydrochloride.** Clinical Pharmacology and Therapeutics. 17(1):1-14, 1975.

The hypnotic drug flurazepam (flurazepam hydrochloride), which was introduced in 1970 and in 1973 accounted for more than 6.5million prescriptions, is examined. Areas covered are: chemical properties, animal pharmacology, pharmacokinetics, clinical uses and effects, flurazepam as a hypnotic, the neurophysiology of sleep, unwanted effects, and the cost of hypnotics. 100 references.

205299 Greenblatt, David J.; Shader, Richard I. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **Drug therapy: benzodiazepines (second of two parts).** New England Journal of Medicine. 291(23):1239-1243, 1974.

The use of benzodiazepines as drug therapy in the treatment of anxiety and other emotional disorders, such as neurotic or reactive depression, and in neuromuscular diseases, seizures, alcohol withdrawal and sleep disorders is examined. The use of benzodiazepines in anesthesia and surgery, in cardioversion, endoscopy, labor and delivery, premedication before general anesthesia and induction is also discussed. The unwanted effects and hazards in the use of benzodiazepines include excessive central nervous system depression, psychiatric reactions, including destructive behavior in some cases, injection site complications, abuse, addiction, and overdose. 14 references.

205586 Pisl, I.; Petranova, T.; Pislova, J. Mental Hospital, Dobrany u Plzne, Czechoslovakia **Simple method for detection of the drug cheaters in psychiatry.** Activitas Nervosa Superior (Praha). 16(3):174, 1974.

At the 16th Annual Psychopharmacological Meeting, a simple and quick method for determining the most often used psychotropic drugs by means of only one test solution was proposed. In phenothiazines (e. g. chlorpromazine, levopromazine, thioridazine, perfenazine, prochlorperazine etc.)three drops of reagent are added to 1 ml urine. Resulting test colors are pink, blue or violet according to the drug and its concentration in the urine. In case of imipramine detection the test reaction is performed with the same reagent, but 20 drops of reagent have to be added to 1 ml of urine. The color is green.

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